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     2003

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     ON 06 MAR 2003
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                E HOFFMANN-LA ROCHE/PA
L1          3315 S E2-E12
L2             2 S L1 AND (PEG-INF? OR PEG(2W)INTERFERON(2W)CONJUGATE?)
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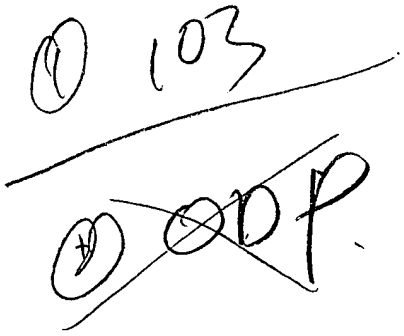

L2 ANSWER 1 OF 2 EUROPATFULL COPYRIGHT 2003 WILA

PATENT APPLICATION - PATENTANMELDUNG - DEMANDE DE BREVET

ACCESSION NUMBER: 809996 EUROPATFULL EW 199749 FS OS
TITLE: Interferon conjugates.
Interferon-Konjugate.
Conjugues de l'interferon.
INVENTOR(S): Bailon, Pascal Sebastian, 21 Woodbine Road, Florham Park, New Jersey 07932, US;
Palleroni, Alicia Vallejo, 47 White Oak Drive, North Caldwell, New Jersey 07006, US
PATENT ASSIGNEE(S): **F. HOFFMANN-LA**
ROCHE AG, 124 Grenzacherstrasse, 4070 Basel, CH
PATENT ASSIGNEE NO: 1107064
OTHER SOURCE: ESP1997073 EP 0809996 A2 971203
SOURCE: Wila-EPZ-1997-H49-T1b
DOCUMENT TYPE: Patent
LANGUAGE: Anmeldung in Englisch; Veroeffentlichung in Englisch
DESIGNATED STATES: R AT; R BE; R CH; R DE; R DK; R ES; R FI; R FR; R GB; R GR; R IE; R IT; R LI; R LU; R MC; R NL; R PT; R SE
PATENT INFO.PUB.TYPE: EPA2 EUROPAEISCHE PATENTANMELDUNG
PATENT INFORMATION:

PATENT NO	KIND	DATE
EP 809996	A2	19971203
'OFFENLEGUNGS' DATE:		19971203
APPLICATION INFO.: EP 1997-108261		19970522
PRIORITY APPLN. INFO.: US 1996-18834		19960531

PA **F. HOFFMANN-LA ROCHE AG**
, 124 Grenzacherstrasse, 4070 Basel, CH
DETDEN. . . case of interferon, PEGylation reduces in vitro antiviral activity but increases antiproliferative activity in human tumor cells. However the new **PEG interferon conjugate** of this invention has surprising properties in that the antiproliferative activity of the PEG interferon is much higher than that not only of interferon but of other **PEG interferon conjugates**. Although the antiproliferative activity of the conjugate is much increased over other **PEG interferon**-.alpha. **conjugates**, yet the reduction in antiviral activity is similar. In addition, the **PEG interferon**-.alpha. **conjugate** of this invention is non-immunogenic, it elicits virtually no antibody formation. In contrast, other **PEG interferon**-.alpha. **conjugates** do elicit limited antibody formation. The conjugate of this invention has the same uses as IFN.alpha., for example, antiproliferative uses. In particular, the **PEG interferon**-.alpha. **conjugates** of this invention are useful to treat immunomodulatory disorders such as neoplastic diseases, for example, hairy cell leukemia, CML, and. . .

L2 ANSWER 2 OF 2 EUROPATFULL COPYRIGHT 2003 WILA

PATENT APPLICATION - PATENTANMELDUNG - DEMANDE DE BREVET

ACCESSION NUMBER: 593868 EUROPATFULL EW 199417 FS OS STA B
TITLE: **PEG-interferon conjugates.**
PEG-Interferon-Konjugate.

Conjugues PEG-interferon.

INVENTOR(S): Karasiewicz, Robert, 30 Deerfield Road, Parsippany, N.J. 07054, US;
Nalin, Carlo, 327 Forest Glenn Avenue, Franklin Lakes, N.J. 07417, US;
Rosen, Perry, 26 Sunset Drive, North Caldwell, N.J. 07006, US

PATENT ASSIGNEE(S): **F. HOFFMANN-LA ROCHE AG**, Grenzacherstrasse 124, CH-4002 Basel, CH

PATENT ASSIGNEE NO: 200573

AGENT: Mezger, Wolfgang, Dr. et al, Grenzacherstrasse 124 Postfach 3255, CH-4002 Basel, CH

AGENT NUMBER: 26171

OTHER SOURCE: ESP1994029 EP 0593868 A1 940427

SOURCE: Wila-EPZ-1994-H17-T1a

DOCUMENT TYPE: Patent

LANGUAGE: Anmeldung in Englisch; Veroeffentlichung in Englisch

DESIGNATED STATES: R AT; R BE; R CH; R DE; R DK; R ES; R FR; R GB; R GR; R IE; R IT; R LI; R LU; R MC; R NL; R PT; R SE

PATENT INFO.PUB.TYPE: EPA1 EUROPAEISCHE PATENTANMELDUNG

PATENT INFORMATION:

PATENT NO	KIND	DATE
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'OFFENLEGUNGS' DATE:		19940427
APPLICATION INFO.: EP 1993-112983		19930813
PRIORITY APPLN. INFO.: US 1992-935770		19920826

GRANTED PATENT - ERTEILTES PATENT - BREVET DELIVRE

ACCESSION NUMBER: 593868 EUROPATFULL EW 199816 FS PS

TITLE: **PEG-interferon conjugates.**
PEG-Interferon-Konjugate.
Conjugues PEG-interferon.

INVENTOR(S): Karasiewicz, Robert, 30 Deerfield Road, Parsippany, N.J. 07054, US;
Nalin, Carlo, 327 Forest Glenn Aven

ACCESSION NUMBER: 593868 EUROPATFULL EW 199417 FS OS STA B
TITLE: **PEG-interferon conjugates.**
PEG-Interferon-Konjugate.
Conjugues PEG-interferon.
INVENTOR(S): Karasiewicz, Robert, 30 Deerfield Road, Parsippany, N.J.
07054, US;
Nalin, Carlo, 327 Forest Glenn Avenue, Franklin Lakes, N.J. 07417, US;
Rosen, Perry, 26 Sunset Drive, North Caldwell, N.J. 07006, US
PATENT ASSIGNEE(S): **F. HOFFMANN-LA ROCHE AG**, Grenzacherstrasse 124,
CH-4002 Basel, CH
PATENT ASSIGNEE NO: 200573
AGENT: Mezger, Wolfgang, Dr. et al, Grenzacherstrasse 124
Postfach 3255, CH-4002 Basel, CH
AGENT NUMBER: 26171
OTHER SOURCE: ESP1994029 EP 0593868 A1 940427
SOURCE: Wila-EPZ-1994-H17-T1a
DOCUMENT TYPE: Patent
LANGUAGE: Anmeldung in Englisch; Veroeffentlichung in Englisch
DESIGNATED STATES: R AT; R BE; R CH; R DE; R DK; R ES; R FR; R GB; R GR; R IE; R IT; R LI; R LU; R MC; R NL; R PT; R SE
PATENT INFO.PUB.TYPE: EPA1 EUROPAEISCHE PATENTANMELDUNG
PATENT INFORMATION:

PATENT NO	KIND	DATE
EP 593868	A1	19940427
'OFFENLEGUNGS' DATE:		19940427
APPLICATION INFO.: EP 1993-112983		19930813
PRIORITY APPLN. INFO.: US 1992-935770		19920826

COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	48.20	758.37

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-1.76	-15.20

S. Jiang
317688
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STRUCTURE FILE UPDATES: 19 APR 2001 HIGHEST RN 331941-31-2
DICTIONARY FILE UPDATES: 19 APR 2001 HIGHEST RN 331941-31-2

TSCA INFORMATION NOW CURRENT THROUGH January 11, 2001

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Structure search limits have been increased. See HELP SLIMIT for details.

```
=> e interferon-.alpha.2a/cn
E1            1     INTERFERON-.ALPHA. R1 RECEPTOR (CATTLE CLONE
BO.ALPHA.RPL/PB
                    LUE)/CN
E2            1     INTERFERON-.ALPHA./.BETA.-BINDING PROTEIN (ECTROMELIA
VIRUS
                    STRAIN MOSCOW GENE C12R)/CN
E3            0 --> INTERFERON-.ALPHA.2A/CN
E4            1     INTERFERON-.ALPHA.2B (PLASMID PMON20442)/CN
E5            1     INTERFERON-.ALPHA.2B (PLASMID PMON30422)/CN
E6            1     INTERFERON-.ALPHA.2B (PLASMID PMON30426)/CN
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E7            1      INTERFERON-.ALPHA.A/D (PLASMID PMON20405)/CN
E8            1      INTERFERON-.ALPHA.A/D (PLASMID PMON20433)/CN
E9            1      INTERFERON-.GAMMA. (CANIS FAMILIARIS)/CN
E10           1      INTERFERON-.GAMMA. (CHICKEN CELL CC8.1H PRECURSOR)/CN
E11           1      INTERFERON-.GAMMA. (HUMAN CHINESE CLONE
PUC19-HIFN-.GAMMA.)/
                     CN
E12           1      INTERFERON-.GAMMA. INDUCIBLE PROTEIN 10 (MOUSE STRAIN
SJL/J
                     SPINAL CORD GENE SCYB10 PRECURSOR)/CN

=> e interferon-.alpha. 2a/cn
E1            1      INTERFERON-.ALPHA. (HAMSTER GENE IFA-3)/CN
E2            1      INTERFERON-.ALPHA. (HUMAN PRECURSOR)/CN
E3            0 --> INTERFERON-.ALPHA. 2A/CN
E4            1      INTERFERON-.ALPHA. R1 RECEPTOR (CATTLE CLONE
BO.ALPHA.RPL/PB
                     LUE)/CN
E5            1      INTERFERON-.ALPHA./.BETA.-BINDING PROTEIN (ECTROMELIA
VIRUS
                     STRAIN MOSCOW GENE C12R)/CN
E6            1      INTERFERON-.ALPHA.2B (PLASMID PMON20442)/CN
E7            1      INTERFERON-.ALPHA.2B (PLASMID PMON30422)/CN
E8            1      INTERFERON-.ALPHA.2B (PLASMID PMON30426)/CN
E9            1      INTERFERON-.ALPHA.A/D (PLASMID PMON20405)/CN
E10           1      INTERFERON-.ALPHA.A/D (PLASMID PMON20433)/CN
E11           1      INTERFERON-.GAMMA. (CANIS FAMILIARIS)/CN
E12           1      INTERFERON-.GAMMA. (CHICKEN CELL CC8.1H PRECURSOR)/CN

=> s interferon-.alpha.?/cn
L4            8 INTERFERON-.ALPHA.?/CN

=> d l3 que stat
L1
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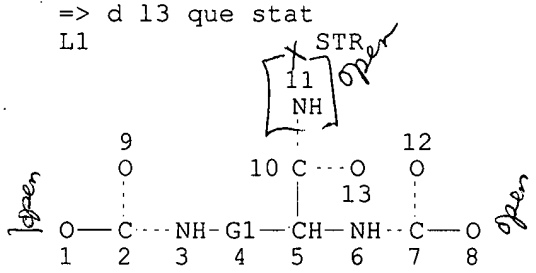
claim 6

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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  13

STEREO ATTRIBUTES: NONE
L3         4070 SEA FILE=REGISTRY SSS FUL L1
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100.0% PROCESSED  23683 ITERATIONS                    4070 ANSWERS
SEARCH TIME: 00.00.04


=> e hepatitis c/cn 5
E1            1     HEPATITIS B VIRUS SURFACE ANTIGEN (HEPATITIS B VIRUS
STRAIN
                    UI004 GENE S)/CN
E2            1     HEPATITIS B VIRUS SURFACE ANTIGEN (HEPATITIS B VIRUS
STRAIN
                    WR2209 GENE S)/CN
E3            0 --> HEPATITIS C/CN
E4            1     HEPATITIS C CORE ANTIGEN (139-ALANINE) (HEPATITIS C
VIRUS)/C
                    N
E5            1     HEPATITIS C CORE ANTIGEN (139-LEUCINE) (HEPATITIS C
VIRUS)/C
                    N

=> e hepatitis c ?/cn 5
E1            1     HEPATITIS B VIRUS SURFACE ANTIGEN (HEPATITIS B VIRUS
STRAIN
                    UI004 GENE S)/CN
E2            1     HEPATITIS B VIRUS SURFACE ANTIGEN (HEPATITIS B VIRUS
STRAIN
                    WR2209 GENE S)/CN
E3            0 --> HEPATITIS C ?/CN
E4            1     HEPATITIS C CORE ANTIGEN (139-ALANINE) (HEPATITIS C
VIRUS)/C
                    N
E5            1     HEPATITIS C CORE ANTIGEN (139-LEUCINE) (HEPATITIS C
VIRUS)/C
                    N

=> e hepatitis c ?/cn
E1            1     HEPATITIS B VIRUS SURFACE ANTIGEN (HEPATITIS B VIRUS
STRAIN
                    UI004 GENE S)/CN
E2            1     HEPATITIS B VIRUS SURFACE ANTIGEN (HEPATITIS B VIRUS
STRAIN
                    WR2209 GENE S)/CN
E3            0 --> HEPATITIS C ?/CN
E4            1     HEPATITIS C CORE ANTIGEN (139-ALANINE) (HEPATITIS C
VIRUS)/C
                    N
E5            1     HEPATITIS C CORE ANTIGEN (139-LEUCINE) (HEPATITIS C
VIRUS)/C
                    N
E6            1     HEPATITIS C CORE ANTIGEN (HEPATITIS B VIRUS PLASMID VECTOR
P
                    THCVC)/CN
E7            1     HEPATITIS C CORE ANTIGEN (HEPATITIS B VIRUS STRAIN ADR
CLONE
                     PPM13 GENE C)/CN
```

```
E8            1     HEPATITIS C CORE ANTIGEN (HEPATITIS C VIRUS CLONE 120NA
N-TE
                    RMINAL FRAGMENT) FUSION PROTEIN WITH HEPATITIS B E ANTIGEN
(
                    HEPATITIS B VIRUS C-TERMINAL FRAGMENT)/CN
E9            1     HEPATITIS C CORE ANTIGEN (HEPATITIS C VIRUS CLONE 120NA)
FUS
                    ION PROTEIN WITH PROTAMINE 1 (MOUSE PRECURSOR)/CN
E10           1     HEPATITIS C CORE ANTIGEN (HEPATITIS C VIRUS CLONE 150NA
N-TE
                    RMINAL FRAGMENT) FUSION PROTEIN WITH HEPATITIS B E ANTIGEN
(
                    HEPATITIS B VIRUS C-TERMINAL FRAGMENT)/CN
E11           1     HEPATITIS C CORE ANTIGEN (HEPATITIS C VIRUS CLONE 150NA
N-TE
                    RMINAL FRAGMENT) FUSION PROTEIN WITH HEPATITIS B E ANTIGEN
(
                    HEPATITIS B VIRUS C-TERMINAL FRAGMENT) FUSION PROTEIN WITH
H
                    EPATITIS C CORE ANTI/CN
E12           1     HEPATITIS C CORE ANTIGEN (HEPATITIS C VIRUS CLONE 24-4
FRAGM
                    ENT)/CN

=> s hepatitis c ?/cn
L5           12 HEPATITIS C ?/CN

=> fil medl,caplus,biosis,embase;s l3 and (l5 or hepatitis c or interferon
alpha or ifn alpha or l4)
COST IN U.S. DOLLARS                              SINCE FILE      TOTAL
                                                     ENTRY    SESSION
FULL ESTIMATED COST                                 145.81     904.18

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TOTAL FOR ALL FILES
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L10 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2001 ACS
1997:457087 Document No. 127:66231 Synthetic peptide substrate for activity assay having chromophore or fluorescent chromophore active against **hepatitis C** virus NS3 protease. Shimizu, Yasuaki; Yamaji, Kayo; Masuho, Yasuhiko; Shimotohno, Kunitada (Rational Drug Design Laboratories, Japan; Shimizu, Yasuaki; Yamaji, Kayo; Masuho, Yasuhiko; Shimotohno, Kunitada). PCT Int. Appl. WO 9719103 A1 19970529, 46 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (Japanese). CODEN: PIXXD2. APPLICATION: WO 1996-JP3398 19961120. PRIORITY: JP 1995-304881 19951122.

AB A synthetic peptide substrate, which contains a specific amino acid sequence, has a fluorescent chromophore or chromophore covalently bonded to the C-terminus, and carries at least one amino acid inhibiting the aminopeptidase digestion on the N-terminal side of the above sequence, is represented by formula Z-Cys-Ala-Met-Ala-X-A-Y (Z = amino acid or peptide residue; X = Leu, Trp, Tyr; A = single bond, peptide; Y = fluorescent chromophore or chromophore; at least one peptide bond present in the Z-Cys region is not easily digested by aminopeptidase and any peptide bond present inside the X-A region is digested by aminopeptidase). A preferred fluorescent chromophore or chromophore is 7-amino-4-methylcoumarin, 7-amino-4-trifluoromethylcoumarin, p-nitroaniline, or .beta.-naphthylamine. The amino acid or amino acid residue present in the Z-Cys region and not readily digested by aminopeptidase is Asp, Ser, Pro, Ile, or Val. An activity assay of **hepatitis C** virus NS3 protease involves double digestion of above synthetic substrate (**hepatitis C** virus NS4A-derived peptide) by **hepatitis C** virus NS3 protease and aminopeptidase. A preferred synthetic substrate is H-Lys-Glu-Asp-Val-Val-Pro-Cys-Ala-Met-Ala-Leu-Y (I; Y = same as above) which maintains digestibility by leucine aminopeptidase (APM) and improves digestion ratio by NS3 protease. The use of this substrate makes it possible to efficiently assay the activity of an NS3 protease and provides a rapid, simple, highly sensitive, and high throughput assay system for NS3 protease which is needed for screening NS3 protease inhibitors. By effecting the assay in the presence of NS4A, the detection sensitivity can be further elevated. Thus, I (Y = p-nitrophenylamino) (II) was prepd. by condensation of Fmoc-Cys(Trt)-Ala-Met-Ala-OH (prepn. given) with H-Leu-NHC6H4NO2-p.HCl and

Fmoc-deprotection followed by condensation of the resulting H-Cys(Trt)-Ala-Met-Ala-Leu-NHC6H4NO2-p with Fmoc-Lys(Boc)-Glu(tBu)-Asp(tBu)-Val-Val-Pro-OH (prepn. given) using DCC in the presence of HOBT in DMF and deprotection. II was digested dose-dependently by maltose binding protein-fused NS3 protease in the presence of NS4A-derived peptide
(H-LTTGSVVIVGRIILSGRPAVVPD-OH) enhancing the activity of NS3 protease.

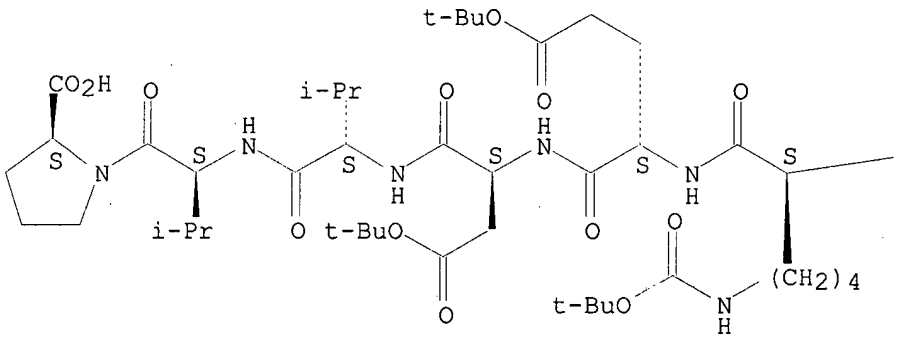
IT **191529-79-0DP**, chlorotrityl resin-bound **191529-79-0P** **191529-82-5P** **191529-89-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of peptides having chromophore or fluorescent chromophore as substrates for assaying **hepatitis C** virus NS3 protease)

RN 191529-79-0 CAPLUS

CN L-Proline, N6-[(1,1-dimethylethoxy)carbonyl]-N2-[(9H-fluoren-9-ylmethoxy)carbonyl]-L-lysyl-L-.alpha.-glutamyl-L-.alpha.-aspartyl-L-valyl-L-valyl-, 2,3-bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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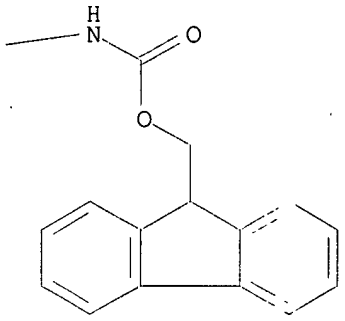
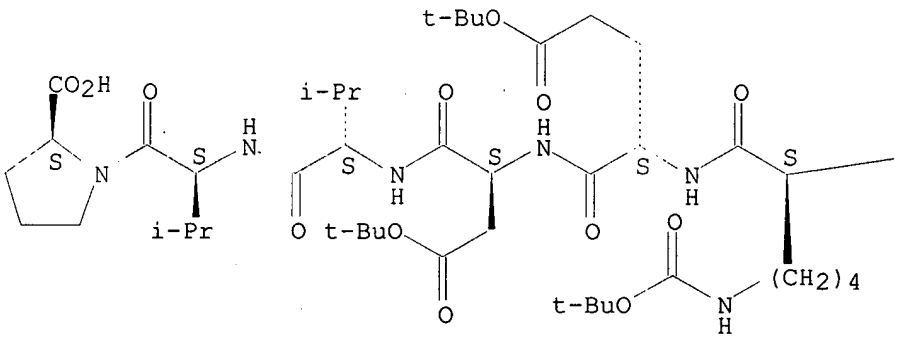


RN 191529-79-0 CAPLUS
CN L-Proline, N6-[(1,1-dimethylethoxy)carbonyl]-N2-[(9H-fluoren-9-ylmethoxy)carbonyl]-L-lysyl-L-.alpha.-glutamyl-L-.alpha.-aspartyl-L-valyl-L-valyl-, 2,3-bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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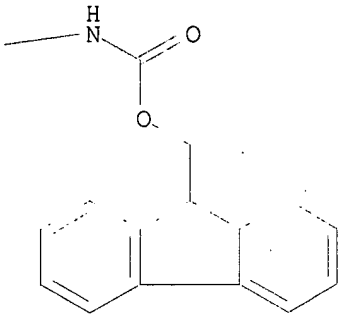
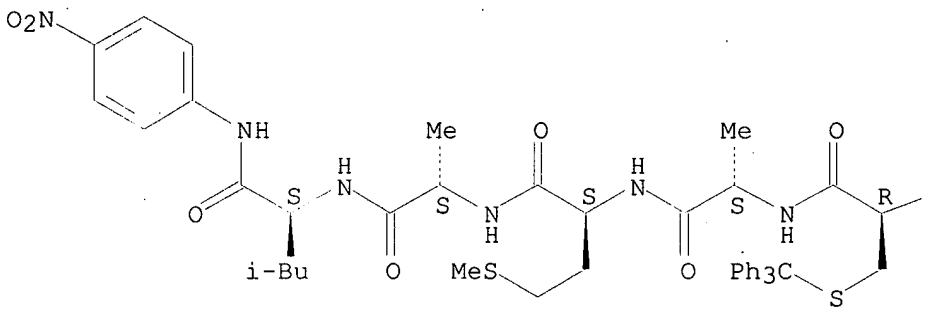


RN 191529-82-5 CAPLUS
CN L-Leucinamide, N6-[(1,1-dimethylethoxy)carbonyl]-N2-[(9H-fluoren-9-ylmethoxy)carbonyl]-L-lysyl-L-.alpha.-glutamyl-L-.alpha.-aspartyl-L-valyl-L-valyl-L-prolyl-S-(triphenylmethyl)-L-cysteinyl-L-alanyl-L-methionyl-L-alanyl-N-(4-nitrophenyl)-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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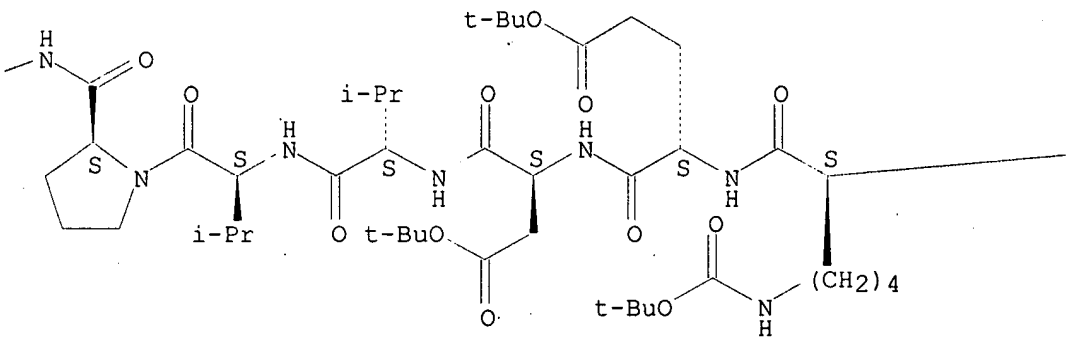

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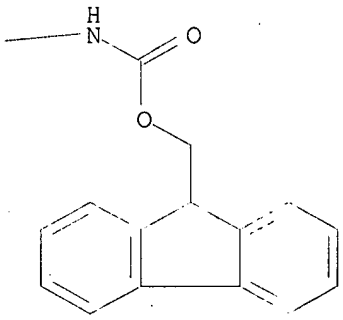

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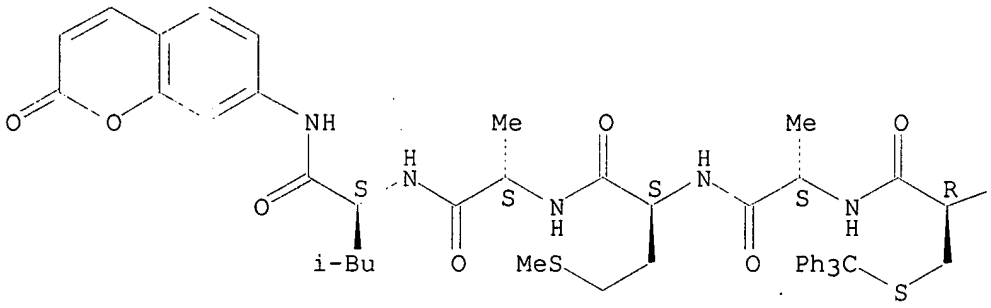
(CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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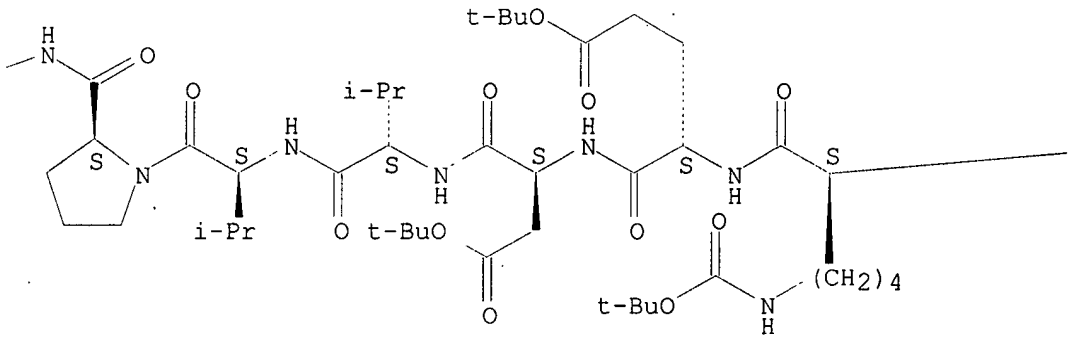

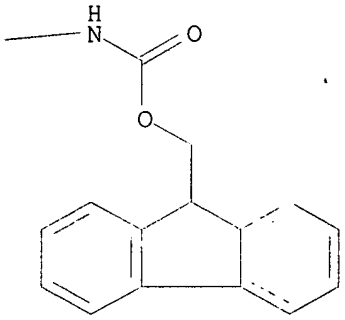

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                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   261.24    1165.42

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for details.

=> e "peg-ifn"/cn 5
E1            1     PEG-DSPE/CN
E2            1     PEG-HT/CN
E3            0 --> PEG-IFN/CN
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E4            1      PEG-SOD/CN
E5            1      PEG2/CN

=> e polyethylene glycol interferon/cn
E1            1      POLYETHYLENE GLYCOL HYDROXYMETHYLPHOSPHONATE/CN
E2            1      POLYETHYLENE GLYCOL IMINOBIS(ETHYLENE) ETHER/CN
E3            0 --> POLYETHYLENE GLYCOL INTERFERON/CN
E4            1      POLYETHYLENE GLYCOL ISO-DODECYLTRIMETHYLOLMETHANE ETHER/CN
E5            1      POLYETHYLENE GLYCOL ISOAMYL THIO ETHER/CN
E6            1      POLYETHYLENE GLYCOL ISOBORNYL ETHER/CN
E7            1      POLYETHYLENE GLYCOL ISOBUTYL ETHER/CN
E8            1      POLYETHYLENE GLYCOL ISOCYANATE/CN
E9            1      POLYETHYLENE GLYCOL ISODECYL ETHER/CN
E10           1      POLYETHYLENE GLYCOL ISODECYL ETHER PHOSPHATE/CN
E11           1      POLYETHYLENE GLYCOL ISODECYL MONOETHER/CN
E12           1      POLYETHYLENE GLYCOL ISONONYLPHENOL ETHER/CN

=> s (peg or polyethylene glycol)(l)(ifn or interferon)
            145 PEG
              2 PEGS
            147 PEG
                  (PEG OR PEGS)
           6314 POLYETHYLENE
          38701 GLYCOL
            715 GLYCOLS
          38701 GLYCOL
                  (GLYCOL OR GLYCOLS)
           5269 POLYETHYLENE GLYCOL
                  (POLYETHYLENE(W)GLYCOL)
             58 IFN
           2393 INTERFERON
              7 INTERFERONS
           2397 INTERFERON
                  (INTERFERON OR INTERFERONS)
L11           0 (PEG OR POLYETHYLENE GLYCOL)(L)(IFN OR INTERFERON)

=> fil medl,caplus,biosis,embase,scisearch,jicst,ntis;s l11
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                              19.62    1185.04

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)    SINCE FILE      TOTAL
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L12           0 FILE MEDLINE
L13           0 FILE CAPLUS
L14           0 FILE BIOSIS
L15           0 FILE EMBASE
L16         110 FILE SCISEARCH
L17           0 FILE JICST-EPLUS
L18           0 FILE NTIS

TOTAL FOR ALL FILES
L19         110 L11

=> s l19 and hepatitis c
L20           0 FILE MEDLINE
L21           0 FILE CAPLUS
L22           0 FILE BIOSIS
L23           0 FILE EMBASE
L24          24 FILE SCISEARCH
L25           0 FILE JICST-EPLUS
L26           0 FILE NTIS

TOTAL FOR ALL FILES
L27          24 L19 AND HEPATITIS C

=> d 1-24 cbib abs
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L27 ANSWER 1 OF 24 SCISEARCH COPYRIGHT 2001 ISI (R)
2001:260966 The Genuine Article (R) Number: 412AR. **PEG**-Intron - Peginterferon alfa-2b powder for injection - Schering-Plough - Pegylated **interferon** for once-weekly treatment of chronic **hepatitis C**. ANON. FORMULARY (MAR 2001) Vol. 36, No. 3, pp. 177-178.
Publisher: ADVANSTAR COMMUNICATIONS. 131 W FIRST ST, DULUTH, MN 55802 USA.
ISSN: 1082-801X. Language: English.

L27 ANSWER 2 OF 24 SCISEARCH COPYRIGHT 2001 ISI (R)
2001:217030 The Genuine Article (R) Number: 407ZW. Current treatment strategies for chronic hepatitis B and C. Lin O S (Reprint); Keeffe E B.
Stanford Univ, Med Ctr, Dept Med, Div Gastroenterol, Stanford, CA 94305 USA (Reprint). ANNUAL REVIEW OF MEDICINE (MAR 2001) Vol. 52, pp. 29-49.

Publisher: ANNUAL REVIEWS. 4139 EL CAMINO WAY, PO BOX 10139, PALO ALTO, CA
94303-0139 USA. ISSN: 0066-4219. Pub. country: USA. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB For chronic hepatitis B, treatment with a 4-month course of **interferon** alfa-2b can achieve hepatitis B e antigen seroconversion, normalization of aminotransferase levels, reduced hepatic inflammation, and possibly reduced progression to cirrhosis and improvement in survival in 20%-30% of patients. Similar results can be achieved with a 12-month course of lamivudine, with response rates increasing to 40%-65% after 3 years of therapy. **Interferon** can also be used in early cirrhotic patients, and lamivudine can be used in advanced cirrhotics and immunosuppressed patients. Combination **interferon** and lamivudine therapy does not confer additional benefits. For chronic **hepatitis C**, the combination of **interferon** alfa-2b and ribavirin is the treatment of choice, offering superior sustained response rates (40%) compared with **interferon** alone (15%). Therapy should be administered for 12 months to patients with genotype 1 virus but for only 6 months to patients with genotypes 2 and 3. Patients experiencing relapse after 6 months of **interferon** monotherapy can be re-treated with **interferon** and ribavirin or high-dose **interferon**, with 45%-56% sustained response rates. However, relatively few patients who are prior nonresponders to **interferon** monotherapy will have sustained response to further **interferon**-based treatments, including combination therapy with ribavirin. Successful therapy not only leads to the eradication of viral RNA but also may delay progression to cirrhosis and hepatocellular carcinoma. **Interferon** combined with **polyethylene glycol** (**PEG**), shows promise as an improved formulation of **interferon** with yet higher sustained response rates.

L27 ANSWER 3 OF 24 SCISEARCH COPYRIGHT 2001 ISI (R)
2001:199190 The Genuine Article (R) Number: 405MR. **PEG-IFN** plus ribavirin for chronic **hepatitis C** - A dose-ranging study of pegylated **interferon** alfa-2b and ribavirin in chronic **hepatitis C** - Glue P, Rouzier-Ranis R, Raffanel C, et al. Hepatology. 2000;32 : 647-653.. ANON. INFECTIONS IN MEDICINE (FEB 2001) Vol. 18, No. 2, pp. 91-92. Publisher: SCP COMMUNICATIONS INC. 134 W 29TH ST, NEW YORK, NY 10001-5304 USA. ISSN: 0749-6524. Language: English.

L27 ANSWER 4 OF 24 SCISEARCH COPYRIGHT 2001 ISI (R)
2001:118527 The Genuine Article (R) Number: 397QF. Efficacy and safety of pegylated (40-kd) interferon alpha-2a compared with interferon alpha-2a in noncirrhotic patients with chronic **hepatitis C**. Reddy K R (Reprint); Wright T L; Pockros P J; Shiffman M; Everson G; Reindollar R; Fried M W; Purdum P P; Jensen D; Smith C; Lee W M; Boyer T D; Lin A; Pedder S; DePamphilis J. Ctr Liver Dis, 1500 NW 12th Ave, Suite 1101, Miami, FL 33136 USA (Reprint); Univ Miami, Sch Med, Miami, FL USA; Vet Adm Med Ctr, San Francisco, CA 94121 USA; Scripps Clin, La Jolla, CA USA; Virginia Commonwealth Univ, Med Coll Virginia, Richmond, VA 23298 USA;

Univ Colorado, Sch Med, Denver, CO USA; Carolinas Ctr Liver Dis, Charlotte, NC USA; Emory Univ, Sch Med, Atlanta, GA USA; Charlotte Clin Gastrointestinal & Liver Dis, Charlotte, NC USA; Rush Presbyterian St Lukes Med Ctr, Chicago, IL 60612 USA; Minnesota Clin Res Ctr, St Paul, MN USA; Univ Texas, SW Med Ctr, Dallas, TX USA; Emory Univ, Sch Med, Atlanta, GA USA; Hoffmann La Roche Inc, Nutley, NJ 07110 USA. HEPATOLOGY (FEB 2001) Vol. 33, No. 2, pp. 433-438. Publisher: W B SAUNDERS CO. INDEPENDENCE SQUARE WEST CURTIS CENTER, STE 300, PHILADELPHIA, PA 19106-3399 USA. ISSN: 0270-9139. Pub. country: USA. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Administration of **interferon** (**IFN**) 3 times weekly in patients with chronic **hepatitis C** (CHC) is associated with low sustained responses, which may be, in part, related to this regimen's inability to maintain **IFN** concentrations sufficient to suppress viral replication. An enhanced **IFN** molecule produced by the covalent attachment of a branched 40-kd **polyethylene glycol** moiety to **IFN** alpha -2a (**PEG**[40kd] **IFN** alpha -2a) exhibits sustained absorption, a restricted volume of distribution, and reduced clearance compared with unmodified **IFN** alpha -2a. One hundred fifty-nine patients with CHC participated in a randomized, ascending-dose (45 or 90, 180, 270 mug) study comparing **PEG**(40kd) **IFN** alpha -2a administered once weekly with 3 MIU **IFN** alpha -2a administered 3 times weekly for 48 weeks to determine the most appropriate **PEG**(40kd) **IFN** alpha -2a dose for subsequent clinical trials. Efficacy was assessed by measuring **hepatitis C** virus (HCV) RNA following a 24-week treatment-free period. Sustained virological responses for **PEG**(40kd) **IFN** alpha -2a once weekly were 10% (45 mug; not significant), 30% (90 mug; P =,009), 36% (180 mug; P = .0006), and 29% (270 mug; P = .004), compared with 3% for the 3-times-weekly 3-MIU **IFN** alpha -2a regimen. The types and frequencies of adverse events and laboratory abnormalities were similar among all groups. In conclusion, once-weekly **PEG**(40kd) **IFN** alpha -2a was associated with a higher number of sustained virological responses compared with **IFN** alpha -2a 3 times weekly in patients with CHC, but had a similar safety profile. The 180-mug **PEG**(40kd) **IFN** alpha -2a dose appeared to be the optimal dose based on sustained virological response and its associated side-effect profile.

L27 ANSWER 5 OF 24 SCISEARCH COPYRIGHT 2001 ISI (R)

2001:16882 The Genuine Article (R) Number: 359PZ. High and low doses of **peg-interferon** alfa 2b plus Ribavirin in "naive" patients with chronic **hepatitis C** genotype 1: Effects on early viral kinetics.. Sanchez-Avila J F (Reprint); Buti M; Martel M; Stalgis C; Lafleur F; Cotrina M; Morral S; Esteban R; Guardia J. Hosp Gen Valle Hebron, Barcelona, Spain; Schering Plough Corp, Res Inst, Kenilworth, NJ 07033 USA. HEPATOLOGY (OCT 2000) Vol. 32, No. 4, Part 2, pp. 359A-359A. MA 800. Publisher: W B SAUNDERS CO. INDEPENDENCE SQUARE

WEST CURTIS CENTER, STE 300, PHILADELPHIA, PA 19106-3399 USA. ISSN: 0270-9139. Pub. country: Spain; USA. Language: English.

L27 ANSWER 6 OF 24 SCISEARCH COPYRIGHT 2001 ISI (R)
2000:918040 The Genuine Article (R) Number: 380PX. Peginterferon alfa-2a in patients with chronic **hepatitis C** and cirrhosis.
Heathcote E J (Reprint); Shiffman M L; Cooksley W G E; Dusheiko G M; Lee S S; Balart L; Reindollar R; Reddy R K; Wright T L; Lin A; Hoffman J; DePamphilis J. TORONTO WESTERN HOSP, UNIV HLTH NETWORK, DEPT MED, 399 BATHURST ST, TORONTO, ON M5T 2S8, CANADA (Reprint); VIRGINIA COMMONWEALTH UNIV, MED COLL VIRGINIA, DEPT MED, HEPATOL SECT, RICHMOND, VA 23298; ROYAL BRISBANE HOSP, DEPT MED, BRISBANE, QLD 4029, AUSTRALIA; ROYAL FREE HOSP, DEPT MED, DEPT CLIN RES, LONDON NW3 2QG, ENGLAND; HERITAGE MED RES CLIN, DEPT MED, CALGARY, AB, CANADA; LOUISIANA STATE UNIV, HLTH SCI CTR, DEPT MED, NEW ORLEANS, LA; CAROLINAS CTR LIVER DIS, DEPT MED, CHARLOTTE, NC; UNIV MIAMI, SCH MED, DEPT MED, CTR LIVER DIS, MIAMI, FL; VET AFFAIRS MED CTR, DEPT MED, GASTROENTEROL UNIT, SAN FRANCISCO, CA 94121; HOFFMANN LA ROCHE INC, NUTLEY, NJ 07110. NEW ENGLAND JOURNAL OF MEDICINE (7 DEC 2000)
Vol. 343, No. 23, pp. 1673-1680. Publisher: MASSACHUSETTS MEDICAL SOC. WALTHAM WOODS CENTER, 860 WINTER ST, WALTHAM, MA 02451-1413. ISSN: 0028-4793. Pub. country: CANADA; USA; AUSTRALIA; ENGLAND. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Background: Chronic **hepatitis C** virus (HCV) infection in patients with cirrhosis is difficult to treat. In patients with chronic **hepatitis C** but without cirrhosis, once-weekly administration of **interferon** modified by the attachment of a 40-kd branched-chain **polyethylene glycol** moiety (peginterferon alfa-2a) is more efficacious than a regimen of unmodified **interferon**. We examined the efficacy and safety of peginterferon alfa-2a in patients with HCV-related cirrhosis or bridging fibrosis.

Methods: We randomly assigned 271 patients with cirrhosis or bridging fibrosis to receive subcutaneous treatment with 3 million units of **interferon** alfa-2a three times weekly (88 patients), 90 microg of peginterferon alfa-2a once weekly (96), or 180 microg of peginterferon alfa-2a once weekly (87). Treatment lasted 48 weeks and was followed by a 24-week follow-up period. We assessed efficacy by measuring HCV RNA and alanine aminotransferase and by evaluating liver-biopsy specimens. A histologic response was defined as a decrease of at least 2 points on the 22-point Histological Activity Index.

Results: In an intention-to-treat analysis, HCV RNA was undetectable at week 72 in 8 percent, 15 percent, and 30 percent of the patients treated with **interferon** alfa-2a and with 90 microg and 180 microg of peginterferon alfa-2a, respectively (P=0.001 for the comparison between 180 microg of peginterferon alfa-2a and **interferon** alfa-2a). At week 72, alanine aminotransferase concentrations had normalized in 15 percent, 20 percent, and 34 percent of patients, respectively (P=0.004 for the comparison between 180 microg of peginterferon alfa-2a and **interferon** alfa-2a). In the subgroup of 184 patients with paired

liver-biopsy specimens, the rates of histologic response at week 72 were 31 percent, 44 percent, and 54 percent, respectively (P=0.02 for the comparison between 180 microg of peginterferon alfa-2a and **interferon** alfa-2a). All three treatments were similarly tolerated.

Conclusions: In patients with chronic **hepatitis C** and cirrhosis or bridging fibrosis, 180 microg of peginterferon alfa-2a administered once weekly is significantly more effective than 3 million units of standard **interferon** alfa-2a administered three times weekly. (N Engl J Med 2000;343:1673-80.) (C) 2000, Massachusetts Medical Society.

L27 ANSWER 7 OF 24 SCISEARCH COPYRIGHT 2001 ISI (R)

2000:918039 The Genuine Article (R) Number: 380PX. Peginterferon alfa-2a in patients with chronic **hepatitis C**. Zeuzem S (Reprint); Feinman S V; Rasenack J; Heathcote E J; Lai M Y; Gane E; OGrady J; Reichen J; Diago M; Lin A; Hoffman J; Brunda M J. UNIV FRANKFURT KLINIKUM, ZENTRUM INNEREN MED, MED KLIN 2, THEODOR STERN KAI 7, D-60590 FRANKFURT, GERMANY (Reprint); MT SINAI HOSP, TORONTO, ON M5G 1X5, CANADA; MED UNIV KLIN, FREIBURG, GERMANY; TORONTO WESTERN HOSP, TORONTO, ON M5T 2S8, CANADA; NATL TAIWAN UNIV HOSP, TAIPEI, TAIWAN; MIDDLEMORE HOSP, AUCKLAND 6, NEW ZEALAND; UNIV LONDON KINGS COLL HOSP, LONDON, ENGLAND; UNIV INST KLIN PHARMAKOL, BERN, SWITZERLAND; GEN UNIV, VALENCIA, SPAIN; HOFFMANN LA ROCHE INC, NUTLEY, NJ 07110. NEW ENGLAND JOURNAL OF MEDICINE (7 DEC 2000) Vol. 343, No. 23, pp. 1666-1672. Publisher: MASSACHUSETTS MEDICAL SOC. WALTHAM WOODS CENTER, 860 WINTER ST, WALTHAM, MA 02451-1413.

ISSN: 0028-4793. Pub. country: GERMANY; CANADA; TAIWAN; NEW ZEALAND; ENGLAND; SWITZERLAND; SPAIN; USA. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Background: Covalent attachment of a 40-kd branched-chain **polyethylene glycol** moiety to **interferon** alfa-2a results in a compound (peginterferon alfa-2a) that has sustained absorption, a slower rate of clearance, and a longer half-life than unmodified **interferon** alfa-2a. We compared the clinical effects of a regimen of peginterferon alfa-2a with those of a regimen of **interferon** alfa-2a in the initial treatment of patients with chronic **hepatitis C**.

Methods: We randomly assigned 531 patients with chronic **hepatitis C** to receive either 180 microg of peginterferon alfa-2a subcutaneously once per week for 48 weeks (267 patients) or 6 million units of **interferon** alfa-2a subcutaneously three times per week for 12 weeks, followed by 3 million units three times per week for 36 weeks (264 patients). All the patients were assessed at week 72 for a sustained virologic response, defined as an undetectable level of **hepatitis C** virus RNA (<100 copies per milliliter).

Results: In the peginterferon group, 223 of the 267 patients completed treatment and 206 completed follow-up. In the **interferon** group, 161 of the 264 patients completed treatment and 154 completed follow-up. In an intention-to-treat analysis in which patients who missed the examination at the end of treatment or follow-up were considered not to have had a response at that point, peginterferon alfa-2a was associated

with a higher rate of virologic response than was **interferon** alfa-2a at week 48 (69 percent vs. 28 percent, P=0.001) and at week 72 (39 percent vs. 19 percent, P=0.001). Sustained normalization of serum alanine aminotransferase concentrations at week 72 was also more common in the peginterferon group than in the **interferon** group (45 percent vs. 25 percent, P=0.001). The two groups were similar with respect to the frequency and severity of adverse events, which were typical of those associated with **interferon** alfa.

Conclusions: In patients with chronic **hepatitis C**, a regimen of peginterferon alfa-2a given once weekly is more effective than a regimen of **interferon** alfa-2a given three times weekly. (N Engl J Med 2000;343:1666-72.) (C) 2000, Massachusetts Medical Society.

L27 ANSWER 8 OF 24 SCISEARCH COPYRIGHT 2001 ISI (R)

2000:681565 The Genuine Article (R) Number: 350FV. A dose-ranging study of pegylated interferon alfa-2b and ribavirin in chronic **hepatitis C**. Glue P (Reprint); RouzierPanis R; Raffanel C; Sabo R; Gupta S K; Salfi M; Jacobs S; Clement R P. SCHERING PLOUGH CORP, RES INST, K-15-4455, 2015 GALLOPING HILL RD, KENILWORTH, NJ 07033 (Reprint); CTR CAP, MONTPELLIER, FRANCE; HOP CAREMEAU, NIMES, FRANCE. HEPATOLOGY (SEP 2000) Vol. 32, No. 3, pp. 647-653. Publisher: W B SAUNDERS CO. INDEPENDENC E SQUARE WEST CURTIS CENTER, STE 300, PHILADELPHIA, PA 19106-3399. ISSN: 0270-9139. Pub. country: USA; FRANCE. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The objectives of this study were to assess the safety, pharmacokinetics, and efficacy of pegylated **interferon** alfa-2b (**PEG**-Intron) plus ribavirin in patients with chronic **hepatitis C**. A total of 72 patients (35 men/37 women, age range 20-68 years) with clinically compensated chronic **hepatitis C** virus (HCV) were enrolled into this open-label, randomized, active controlled study. Patients received either **PEG**-Intron 0.35, 0.7, or 1.4 mu g/kg subcutaneously weekly for 24 weeks alone, or in combination with ribavirin 600, 800, or 1,000 to 1,200 mg orally daily. Patients were evaluated during treatment and after a 24-week follow-up period for safety and efficacy. Detailed pharmacokinetic assessments were performed at weeks 1 and 4. **PEG**-Intron alone produced expected dose-related reductions in white cells, neutrophils and platelets. Addition of ribavirin reduced hemoglobin levels in a dose-related manner, did not further reduce **PEG**-Intron-induced decreases in neutrophil or white cell count, and increased platelet counts. Neutrophil function tests (C5a and FMLP migration, killing curves) were unaltered. Reported adverse events (flu-like symptoms, asthenia) were qualitatively similar in all dose groups. Anti-HCV activity, as measured by loss of detectable serum HCV RNA (i.e. <100 copies/mL) at the end of treatment (week 24) and after 24 weeks of follow-up (week 48) showed dose-response trends for **PEG**-Intron. At each **PEG** -Intron dose level, anti-HCV activity was higher in patients coadministered ribavirin than in patients treated with **PEG** -Intron monotherapy. There was no evidence of pharmacokinetic interactions

with either drug. We conclude that the safety and tolerability of combined **PEG**-Intron/ribavirin and **PEG**-Intron alone were comparable. Combined **PEG**-Intron/ribavirin showed dose-related synergistic anti-HCV effects, which were numerically superior to those obtained with **PEG**-Intron monotherapy.

L27 ANSWER 9 OF 24 SCISEARCH COPYRIGHT 2001 ISI (R)
2000:591637 The Genuine Article (R) Number: 315GP. Evaluation of the safety and efficacy of once-weekly **peg/interferon** alfa-2a (PEGASYS(TM)) for chronic **hepatitis C**. A multinational, randomized study. Zeuzem S (Reprint); Feinman S V; Rasenack J; Heathcote E J; Lai M Y; Gane E; OGrady J; Reichen J; Brunda M J. JOURNAL OF HEPATOLOGY (MAR 2000) Vol. 32, Supp. [2], pp. 29-29. Publisher: MUNKSGAARD INT PUBL LTD. 35 NORRE SOGADE, PO BOX 2148, DK-1016 COPENHAGEN, DENMARK. ISSN: 0168-8278. Language: English.

L27 ANSWER 10 OF 24 SCISEARCH COPYRIGHT 2001 ISI (R)
2000:591636 The Genuine Article (R) Number: 315GP. Pegylated **interferon** alfa-2b (**PEG**-Intron) monotherapy is superior to **interferon** alfa-2b (Intron A) for the treatment of chronic **hepatitis C**. Trepo C (Reprint); Lindsay K; Niederau C; Shiffman M; Gordon S; Hoefs J; Schiff E; Marcellin P; Bacon B; Fang J; Garaud J; Albrecht J. HOP HOTEL DIEU, F-69288 LYON, FRANCE; SCHERING PLOUGH RES INST, KENILWORTH, NJ 07033. JOURNAL OF HEPATOLOGY (MAR 2000) Vol. 32, Supp. [2], pp. 29-29. Publisher: MUNKSGAARD INT PUBL LTD. 35 NORRE SOGADE, PO BOX 2148, DK-1016 COPENHAGEN, DENMARK. ISSN: 0168-8278. Pub. country: FRANCE; USA. Language: English.

L27 ANSWER 11 OF 24 SCISEARCH COPYRIGHT 2001 ISI (R)
2000:492311 The Genuine Article (R) Number: 327VW. Therapeutic options for HCV - management of the infected individual. Foster G R (Reprint). ST MARYS HOSP, IMPERIAL COLL SCH MED, DEPT MED, CTR LIVER, QEQM WING, PRAED ST, LONDON W2 1PG, ENGLAND (Reprint). BEST PRACTICE & RESEARCH IN CLINICAL GASTROENTEROLOGY (APR 2000) Vol. 14, No. 2, pp. 255-264. Publisher: BAILLIERE TINDALL. 24-28 OVAL RD, LONDON NW1 7DX, ENGLAND. ISSN: 1521-6918
. Pub. country: ENGLAND. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Patients with chronic **hepatitis C** infection should be assessed by liver biopsy prior to consideration of anti-viral therapy. Patients with histologically mild disease should be observed at regular intervals and assessed with a repeat liver biopsy after an interval of 3-4 years. Those with severe disease should receive early treatment with **interferon**-se and ribavirin. The duration of therapy is determined by the genotype of the infecting virus-viral genotypes 2 and 3 require only 6 months of treatment but other genotypes should be treated for 12 months. Approximately 35-40% of treated patients will respond to therapy with a permanent cessation of viral replication and improvement in liver histology. New therapies including **polyethylene glycol**, PEGylated, **interferons** and combination regimes involving amantadine are currently under evaluation and it is hoped that improved regimes will be developed in the near future.

L27 ANSWER 12 OF 24 SCISEARCH COPYRIGHT 2001 ISI (R)
2000:478129 The Genuine Article (R) Number: 327KB. Coinfection by HIV and **hepatitis C** virus. Perronne C (Reprint); BaniSadr F. HOP UNIV RAYMOND POINCARE, FAC MED PARIS OUEST, SERV MALAD INFECT & TROP, F-92380 GARCHES, FRANCE (Reprint). MEDECINE ET MALADIES INFECTIEUSES (JUN 2000) Vol. 30, No. 6, pp. 344-346. Publisher: EDITIONS SCIENTIFIQUES MEDICALES ELSEVIER. 23 RUE LINOIS, 75724 PARIS CEDEX 15, FRANCE. ISSN: 0399-077X. Pub. country: FRANCE. Language: French.

L27 ANSWER 13 OF 24 SCISEARCH COPYRIGHT 2001 ISI (R)
2000:400449 The Genuine Article (R) Number: 317AC. Antiviral therapy of **hepatitis C**. Erhardt A (Reprint); Petry W; Ebel M; Jablonowski H; Heintges T; Haussinger D. UNIV DUSSELDORF, KLIN GASTROENTEROL HEPATOL & INFEKTIOL, MOORENSTR 5, D-40225 DUSSELDORF, GERMANY (Reprint). ZEITSCHRIFT FUR GASTROENTEROLOGIE (MAR 2000) Vol. 38, No. 3, pp. 259-269. Publisher: DEMETER VERLAG GEORG THIEME VERLAG. PETRA SCHLAGENHAUF, RUDIGERSTR 14, D-70469 STUTTGART, GERMANY. ISSN: 0044-2771.
Pub. country: GERMANY. Language: German.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB **Hepatitis C** is one of the world's leading infectious diseases. The **interferon**-ribavirin combination therapy is the new standard for the treatment of **hepatitis C** in naive and relapse patients. Virological sustained response rates can be more than doubled by the **IFN**-ribavirin combination therapy compared to **IFN**-monotherapy and treatment duration can be reduced to six months in many cases. The **IFN**-ribavirin combination therapy has a high relative benefit in patients with unfavorable predictive parameters like high viral load, HCV genotype-1 infection and compensated Liver cirrhosis. Anemia is the most important side effect of the guanosin analogue ribavirin. There - are no official therapeutic recommendations for non-responder patients at present. These patients should be treated within controlled clinical trials. Monotherapy with **PEG**(pegylated)-**interferons** and combination therapies with **PEG-interferons** and ribavirin are the most promising future therapeutic options.

L27 ANSWER 14 OF 24 SCISEARCH COPYRIGHT 2001 ISI (R)
2000:282192 The Genuine Article (R) Number: 301NV. Coinfection with the **hepatitis C** virus and HIV: current aspects. BaniSadr F (Reprint); Perronne C. HOP UNIV RAYMOND POINCARE, FAC MED PARIS OUEST, SERV MALAD INFECT & TROP, 104 BLVD RAYMOND POINCARE, F-92380 GARCHES, FRANCE (Reprint). MEDECINE ET MALADIES INFECTIEUSES (MAR 2000) Vol. 30, Supp. [1], pp. S43-S48. Publisher: EDITIONS SCIENTIFIQUES MEDICALES ELSEVIER. 23 RUE LINOIS, 75724 PARIS CEDEX 15, FRANCE. ISSN: 0399-077X. Pub. country: FRANCE. Language: French.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB The treatment of coinfection with the **hepatitis C** virus (HCV) in HIV-infected patients was rarely discussed before the era of the HIV protease inhibitors, since the response to monotherapy with **interferon** alpha (INF alpha) was poor, with a mean prognosis of the HIV disease estimated at around ten years. In the present context, monitoring is reconsidered. The HIV-associated immunosuppression may be responsible fora false negativity of some serologic tests for HCV. The

HIV-HCV coinfection increases the risk of maternofoetal transmission of HCV. Studies evaluating the influence of the HIV coinfection on the natural history of the HCV infection show its deleterious role. The immune restoration obtained with the highly active antiretroviral therapies is not linked with a decrease of the HCV viral load. The HIV-HCV coinfection is responsible for a threefold increase of the risk of elevation of seric transaminases when an antiretroviral treatment is given. The immune restoration obtained with an antiretroviral treatment may reveal the HCV infection and favor a rapid aggravation of hepatic histology and evolution toward cirrhosis. HCV-associated complications may become a major factor of morbidity and mortality, leading to the need for an anti-**hepatitis C** treatment in HIV-infected patients. The combination of INF alpha and ribavirin seems to be the best treatment, Its efficacy and tolerability must be evaluated in HIV-infected patients. Drug interactions are likely to occur, and INF alpha, like ribavirin, may favor CD4 lymphopenia. A new form of INF alpha with a prolonged half-life (**PEG**-INF alpha) seems to be promising. (C) 2000 Editions scientifiques et medicales Elsevier SAS.

L27 ANSWER 15 OF 24 SCISEARCH COPYRIGHT 2001 ISI (R)
2000:235966 The Genuine Article (R) Number: 295LU. Pathogenesis, diagnosis and management of **hepatitis C**. Boyer N; Marcellin P (Reprint). HOP BEAUJON, SERV HEPATOL, CTR RECH CLAUDE BERNARD HEPATITES VIRALES, 100 BD GEN LECLERC, F-92110 CLICHY, FRANCE (Reprint); HOP BEAUJON, SERV HEPATOL, CTR RECH CLAUDE BERNARD HEPATITES VIRALES, F-92110 CLICHY, FRANCE; HOP BEAUJON, INSERM, U481, F-92110 CLICHY, FRANCE. JOURNAL OF HEPATOLOGY (JAN 2000) Vol. 32, Supp. [1], pp. 98-112. Publisher: MUNKSGAARD INT PUBL LTD. 35 NORRE SOGADE, PO BOX 2148, DK-1016 COPENHAGEN, DENMARK. ISSN: 0168-8278. Pub. country: FRANCE. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB The **hepatitis C** virus (HCV) is the leading cause of chronic liver disease worldwide. It is estimated that about 170 million people are chronically infected with HCV. Chronic **hepatitis C** is a major cause of cirrhosis and hepatocellular carcinoma and HCV-related endstage liver disease is, in many countries, the first cause of liver transplantation.

HCV infection is characterized by its propensity to chronicity. Because of its high genetic variability, HCV has the capability to escape the immune response of the host. HCV is not directly cytopathic and liver lesions are mainly related to immune-mediated mechanisms, which are characterized by a predominant type 1 helper cell response. Co-factors influencing the outcome of the disease including age, gender and alcohol consumption are poorly understood and other factors such as immunologic and genetic factors may play an important role.

Recent studies have shown that the combination therapy with alpha **interferon** and ribavirin induces a sustained virological response in about 40% of patients with chronic **hepatitis C**. The

sustained response rates are mainly dependent on the viral genotype (roughly 60% in genotype non-1 and 30% in genotype 1).

Reliable diagnostic tools are now available and useful for detecting HCV infection, to quantify viral load and to determine the viral type. The assessment of the viral quasispecies and the characterization of viral sequences might be clinically relevant but standardized and simple techniques are needed.

The lack of animal models and of in vitro culture systems hampers the understanding of the pathogenesis of chronic **hepatitis C** and the development of new antivirals. New therapeutic schedules with higher and/or daily doses of alpha **interferon** do not seem to improve the efficacy greatly. The conjugation with **polyethylene glycol** (**PEG**) improved the pharmacodynamics and the efficacy of alpha **interferon**.

Emerging new therapies include inhibitors of viral enzymes (protease, helicase and polymerase), cytokines (IL-12 and IL-10), antisense oligonucleotides rand ribozymes. The first candidate compounds should be available in the next few years.

The development of an effective vaccine remains the most difficult and pressing challenge. Because of the high protein variability of HCV, protective vaccines could be extremely difficult to produce and therapeutic vaccines seem more realistic.

Considerable progress has been made in the held of HCV since its discovery 10 years ago but a major effort needs to be made in the next decade to control HCV-related liver disease.

L27 ANSWER 16 OF 24 SCISEARCH COPYRIGHT 2001 ISI (R)

1999:937758 The Genuine Article (R) Number: 260TU. Characteristics of **hepatitis C**-virus and viral predictors of therapeutical response. Ambrosch A (Reprint); Konig W. UNIV KLIN, INST MIKROBIOL, LEIPZIGER STR 44, D-39120 MAGDEBURG, GERMANY (Reprint); OTTO VON GUERICKE UNIV, INST MIKROBIOL, MAGDEBURG, GERMANY. MEDIZINISCHE KLINIK (15 NOV 1999) Vol. 94, No. 11, pp. 626-632. Publisher: URBAN & VOGEL. LINDWURMSTRASSE 95, D-80337 MUNICH, GERMANY. ISSN: 0723-5003. Pub. country: GERMANY. Language: German.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB square Natural History of **Hepatitis C**-Infection and Viral Characteristics: **Hepatitis C**-virus (HCV) infection is a major cause of non-A, non-B-hepatitis and, additionally, is associated with liver cirrhosis and hepato-cellular carcinoma. The high degree of chronificity of HCV-infection is reasonable due to antigenic variability of neutralizing epitopes leading to incomplete immunoresponse with sublity of neutralizing epitopes leading to incomplete immunoresponce with subsequent virus persistence. Besides genetic variants of HCV within a virus population (quasispecies nature of HCV), different genotypes are classified being genetically and phenotypically distinct, and geographically restricted in part. Genotyping of HCV is not only important for phylogenetic and epidemiological studies, but also a prodictive marker for pathogenesis and therapy.

square Viral Predictors of HCV Therapy: In a meta-analysis of 18 therapeutical studies of chronical HCV infections, genotype 1 and high levels of viremia determined markedly the response to **interferon** therapy. In this context, clinical trials have proven the effect of a combined therapy with **interferon** and ribavirin. Especially patients with HCV genotype 1 or high levels of viremia had a real benefit from combined antiviral therapy in comparison to monotherapy with **interferon**.

square Conclusion and Future Concepts: Besides recent concepts improving the therapeutical response to HCV infection, further effort is necessary to develop more successful strategies for eradication of **hepatitis C** virus. In this context, variations of **interferon** therapy should be evaluated (e.g. higher and daily doses, longer duration of **interferon** therapy, ''retarded'' **interferon** (**PEG-IFN**). In addinon, new therapeutical concepts should be performed including a combination of **interferon** with other known antiviral agents (amantadine), a combination with immunomodulators (GM-CSF, thymosin alpha 1), the development of new antiviral agents (inhibitors of viral proteases, helicases and polymerases) and the exploration of anti-viral, molecular strategies (specific ribozymes, antisense oligonucleotides and DNA-vaccination). Nevertheless, the development of an effective vaccination should be the most important challenge for the future.

L27 ANSWER 17 OF 24 SCISEARCH COPYRIGHT 2001 ISI (R)
1999:878608 The Genuine Article (R) Number: 239XE. Community-based treatment of patients with chronic **hepatitis C** using peginterferon alpha-2a (**PEG-IFN**): One center's experience.. Reindollar R (Reprint); Purdum P; Thompson E; Hudson M; Johnston P; Depamphilis J; Brunda M. CHARLOTTE CLIN GASTROINTESTINAL & LIVER DIS, NUTLEY, NJ; HOFFMANN LA ROCHE INC, NUTLEY, NJ 07110. HEPATOLOGY (OCT 1999) Vol. 30, No. 4, Part 2, Supp. [S], pp. 1820-1820. Publisher: W B SAUNDERS CO. INDEPENDENCE SQUARE WEST CURTIS CENTER, STE 300, PHILADELPHIA, PA 19106-3399. ISSN: 0270-9139. Pub. country: USA. Language: English.

L27 ANSWER 18 OF 24 SCISEARCH COPYRIGHT 2001 ISI (R)
1999:877416 The Genuine Article (R) Number: 239XE. Multinational evaluation of the efficacy and safety of once-weekly peginterferon alpha-2A (**PEG-IFN**) in patients with chronic **hepatitis C** (CHC) with compensated cirrhosis.. Heathcote E J (Reprint); Shiffman M L; Cooksley G; Dusheiko G M; Lee S S; Balart L; Reindollar R; Reddy R; Wright T; Dephamphilis J. TORONTO WESTERN HOSP, TORONTO, ON M5T 2S8, CANADA; VIRGINIA COMMONWEALTH UNIV, MED COLL VIRGINIA, RICHMOND, VA 23298; ROYAL BRISBANE HOSP, BRISBANE, QLD 4029, AUSTRALIA; ROYAL FREE HOSP, LONDON NW3 2QG, ENGLAND; HERITAGE MED RES CLIN, CALGARY, AB, CANADA; MEM MED CTR, NEW ORLEANS, LA; CHARLOTTE CLIN GASTROINTESTINAL & LIVER DIS, CHARLOTTE, NC; UNIV MIAMI, SCH MED, MIAMI, FL; UNIV CALIF SAN FRANCISCO, SAN FRANCISCO, CA 94143; HOFFMANN LA ROCHE INC, ROCHE PEGINTERFERON ALPHA 2A INT STUDY GRP, NUTLEY, NJ 07110. HEPATOLOGY (OCT 1999) Vol. 30, No. 4,

Part 2, Supp. [S], pp. 621-621. Publisher: W B SAUNDERS CO. INDEPENDENCE SQUARE WEST CURTIS CENTER, STE 300, PHILADELPHIA, PA 19106-3399. ISSN: 0270-9139. Pub. country: CANADA; USA; AUSTRALIA; ENGLAND. Language: English.

L27 ANSWER 19 OF 24 SCISEARCH COPYRIGHT 2001 ISI (R)
1999:876939 The Genuine Article (R) Number: 239XE. Combination therapy with peginterferon alpha-2a (**PEG-IFN**) and ribavirin in the treatment of patients with chronic **hepatitis C** (CHC): A phase II open-label study. Sulkowski M (Reprint); Reindollar R; Yu J. JOHNS HOPKINS UNIV, SCH MED, BALTIMORE, MD; CHARLOTTE CLIN GASTROINTESTINAL & LIVER DIS, CHARLOTTE, NC; HOFFMANN LA ROCHE INC, NUTLEY, NJ 07110. HEPATOLOGY (OCT 1999) Vol. 30, No. 4, Part 2, Supp. [S], pp. 145-145. Publisher: W B SAUNDERS CO. INDEPENDENCE SQUARE WEST CURTIS CENTER, STE 300, PHILADELPHIA, PA 19106-3399. ISSN: 0270-9139. Pub. country: USA. Language: English.

L27 ANSWER 20 OF 24 SCISEARCH COPYRIGHT 2001 ISI (R)
1999:876914 The Genuine Article (R) Number: 239XE. A branched methoxy 40 KDA **polyethylene glycol** (**PEG**) moiety optimizes the pharmacokinetics (PK) of peginter-feron alpha-2A (**PEG-IFN**) and may explain its enhanced efficacy in chronic **hepatitis C** (CHC).. Algranati N E (Reprint); Sy S; Modi M. HOFFMANN LA ROCHE INC, NUTLEY, NJ 07110. HEPATOLOGY (OCT 1999) Vol. 30, No. 4, Part 2, Supp. [S], pp. 120-120. Publisher: W B SAUNDERS CO. INDEPENDENCE SQUARE WEST CURTIS CENTER, STE 300, PHILADELPHIA, PA 19106-3399. ISSN: 0270-9139. Pub. country: USA. Language: English.

L27 ANSWER 21 OF 24 SCISEARCH COPYRIGHT 2001 ISI (R)
1999:691833 The Genuine Article (R) Number: 232MG. Developments in **hepatitis C** during 1997-1999. Poordad F F (Reprint); Gish R G. JOHNS HOPKINS UNIV, SCH MED, DEPT MED, DIV GASTROENTEROL, 1830 E MONUMENT ST, 423, BALTIMORE, MD 21205 (Reprint). EXPERT OPINION ON THERAPEUTIC PATENTS (SEP 1999) Vol. 9, No. 9, pp. 1249-1262. Publisher: ASHLEY PUBL LTD. 1ST FL, THE LIBRARY, 1 SHEPHERDS HILL HIGHGATE, LONDON N6 5QJ, ENGLAND. ISSN: 1354-3776. Pub. country: USA. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB **Hepatitis C** has became an area of intensive research over the past several years. With current worldwide prevalence estimated at 150 to 200 million people, and with almost four million Americans infected, ii is a major public health issue [1]. Of those infected, over 85% will develop chronic infection [2,3]. of those who develop chronic infection, 20% will develop cirrhosis, and in the cirrhotic population, 20% develop hepatocellular carcinoma [4]. It is still difficult in the early stages of disease to determine who is at risk of developing cirrhosis, and therefore who would benefit most from therapy. manifestations of the disease that lead clinicians to initiate therapy [5]. The However, even in the non-cirrhotic individual, there are many symptomatic ultimate goal of treatment is to achieve sustained eradication of the virus. Until recently, the mainstay of treatment has

been interferon (IFN-) monotherapy, which is less than 25% effective and is generally accompanied by side effects. Newer therapeutic modalities focus on less toxic compounds, targeting viral proteins such as protease or helicase, or viral genomic segments with antisense peptides and ribozymes. This chapter is an overiview of the patent literature from 1997 to mid-1999 and discusses possible new treatement options including vaccines and delivery systems to cells (Figure 1).

L27 ANSWER 22 OF 24 SCISEARCH COPYRIGHT 2001 ISI (R)
1999:626397 The Genuine Article (R) Number: 224LA. Detection and characterization of antibodies to **PEG-IFN**-alpha 2b using surface plasmon resonance. Takacs M A; Jacobs S J (Reprint); Bordens R M; Swanson S J. SCHERING PLOUGH CORP, RES INST, 2015 GALLOPING HILL RD, MSK-15-2700, KENILWORTH, NJ 07033 (Reprint); SCHERING PLOUGH CORP, RES INST, KENILWORTH, NJ 07033. JOURNAL OF INTERFERON AND CYTOKINE RESEARCH (JUL 1999) Vol. 19, No. 7, pp. 781-789. Publisher: MARY ANN LIEBERT INC PUBL. 2 MADISON AVENUE, LARCHMONT, NY 10538. ISSN: 1079-9907.
Pub. country: USA. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Some patients treated with type I **interferon** (**IFN**) preparations develop neutralizing antibodies that may abrogate any clinical benefit. We have a new complex of **polyethylene glycol**(12000) and **IFN**-alpha 2b (**PEG-IFN**-alpha 2b) in clinical trials and need to be able to detect any antibodies formed specifically against the complex, We have, therefore, devised a method based on measurement of surface plasmon resonance (SPR) in the BIACORE 2000(TM) apparatus. **PEG-IFN**-alpha 2b is anchored to one flow cell on the sensor chip, **IFN**-alpha 2b to another, and **PEG** to a third. A 20 mu l serum sample flows in turn through the three cells, which are optically scanned. Any antibodies in the serum bind to the corresponding immobilized antigen, and a change in the optical signal is generated. With appropriate specific reagents, their immunoglobulin isotype can be similarly established. The automated assay can quickly test numerous sera. Very little serum is needed, and the assay is reliable and precise and can detect low-affinity antibodies.

L27 ANSWER 23 OF 24 SCISEARCH COPYRIGHT 2001 ISI (R)
1999:448118 The Genuine Article (R) Number: 187GJ. A controlled, randomized, multicenter, descending dose phase II trial of pegylated **interferon** alfa-2a (**PEG**) vs standard **interferon** alfa-2a (**IFN**) for treatment of chronic **hepatitis C**. Shiffman M (Reprint); Pockros P J; Reddy R K; Wright T L; Reindollar R; Fried M W; Purdum P P; Everson G; Pedder S. VIRGINIA COMMONWEALTH UNIV, MED COLL VIRGINIA, RICHMOND, VA 23298; SCRIPPS CLIN & RES INST, LA JOLLA, CA; VET AFFAIRS MED CTR, SAN FRANCISCO, CA 94121; UNIV MIAMI, MIAMI, FL 33152; CHARLOTTE CLIN, CHARLOTTE, ND; UNIV N CAROLINA, CHAPEL HILL, NC; UNIV COLORADO, DENVER, CO 80202; F HOFFMANN LA ROCHE & CO LTD, PEG IFN ALFA 2A CLIN STUDY GRP, NUTLEY, NJ. GASTROENTEROLOGY (APR 1999) Vol. 116, No. 4, Part 2, pp. L0418-L0418. Publisher: W B SAUNDERS CO

. INDEPENDENCE SQUARE WEST CURTIS CENTER, STE 300, PHILADELPHIA, PA 19106-3399. ISSN: 0016-5085. Pub. country: USA. Language: English.

L27 ANSWER 24 OF 24 SCISEARCH COPYRIGHT 2001 ISI (R)
1999:445782 The Genuine Article (R) Number: 187GJ. The pharmacokinetics of pegylated-40K **interferon** alfa-2a (**PEG-IFN**)
in chronic **hepatitis C** (CHC) patients with cirrhosis.
Heathcote E J (Reprint); Pockros P J; Fried M W; Bain M A; DePamphilis J; Modi M. TORONTO HOSP, TORONTO, ON M5T 2S8, CANADA; SCRIPPS CLIN & RES INST, LA JOLLA, CA; UNIV N CAROLINA, CHAPEL HILL, NC; F HOFFMANN LA ROCHE LTD, PEG IFN ALFA CLIN STUDY GRP A, NUTLEY, NJ. GASTROENTEROLOGY (APR 1999
) Vol. 116, No. 4, Part 2, pp. G3190-G3190. Publisher: W B SAUNDERS CO. INDEPENDENCE SQUARE WEST CURTIS CENTER, STE 300, PHILADELPHIA, PA 19106-3399. ISSN: 0016-5085. Pub. country: CANADA; USA. Language: English.

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DICTIONARY FILE UPDATES: 19 APR 2001 HIGHEST RN 331941-31-2

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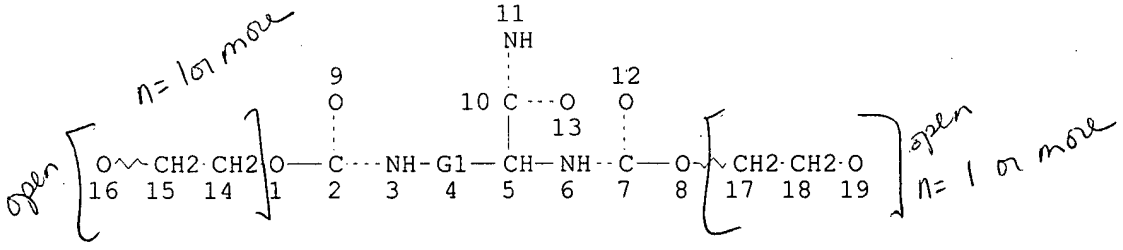
L28 STR



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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 19

STEREO ATTRIBUTES: NONE
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100.0% PROCESSED 528 ITERATIONS 5 ANSWERS
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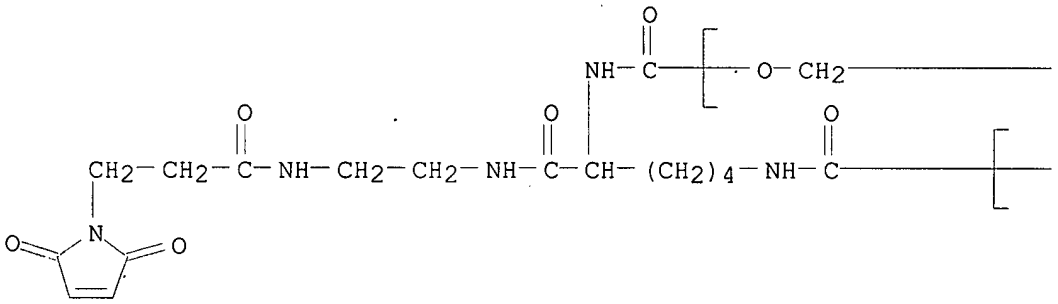
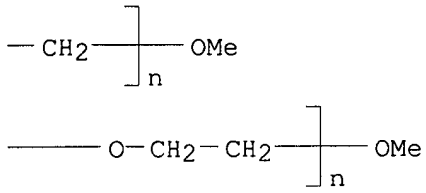
L30 ANSWER 1 OF 5 REGISTRY COPYRIGHT 2001 ACS
RN 322725-90-6 REGISTRY
CN Poly(oxy-1,2-ethanediyl),
.alpha.,.alpha.'-[[(1S)-1-[[[2-[[3-(2,5-dihydro-
2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]amino]ethyl]amino]carbonyl]-1,5-
pentanediyl]bis(iminocarbonyl)]bis[.omega.-methoxy- (9CI) (CA INDEX
NAME)
MF (C2 H4 O)n (C2 H4 O)n C19 H29 N5 O8
CI PMS
PCT Polyether
SR CA
LC STN Files: CA, CAPLUS

PAGE 1-A





2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:143876 Protease conjugates having sterically protected epitope regions and their uses in cleaning and personal care compositions.
Rubingh, Donn Nelton; Weisgerber, David John; Correa, Paul Elliott (The Procter & Gamble Company, USA). PCT Int. Appl. WO 2001007577 A2 20010201,
40 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG,
BR, BY, BZ, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US18854 20000711. PRIORITY: US 1999-PV144979 19990722.
AB The present disclosure relates to subtilisin protease conjugate comprising
a protease moiety and one or more addn. moieties. Each addn. moiety is covalently attached to an epitope protection position of the protease moiety. The protease conjugates have decreased immunogenicity relative to
a parent protease. The present disclosure further relates to cleaning and
personal care compns. comprising the protease conjugates.

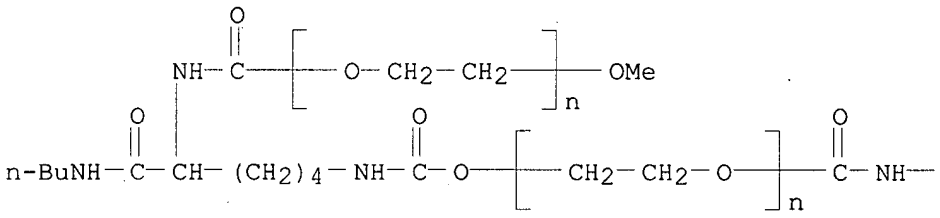
REFERENCE 2: 134:143874 Protease conjugates having sterically protected clip
sites and reduced immunogenicity and their use in cleaning and personal care compositions. Weisgerber, David John; Rubingh, Donn Nelton; Correa, Paul Elliott (The Procter & Gamble Company, USA). PCT Int. Appl. WO 2001007484 A2 20010201, 38 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT,
AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES,

FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US18855 20000711. PRIORITY: US 1999-PV144981 19990722.

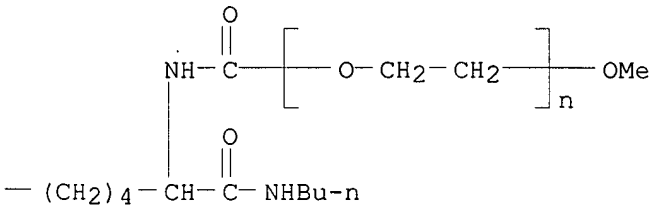
AB The present disclosure relates to subtilisin protease conjugate comprising a protease moiety and one or more addn. moieties. Each addn. moiety is covalently attached to a clip site protection position of the protease moiety, wherein the clip site protection positions are selected from 13, 14, 15, 16, 18, 19, 20, 21, 84, 85, 88, 158, 159, 160, 161, 162, 163, 164, 165, 170, 186, 191, 192, 193, 194, 196, 259, 260, 261, 262, and 274 corresponding to subtilisin BPN'. The protease conjugates have decreased immunogenicity relative to a parent protease. The present disclosure further relates to cleaning and personal care compns. comprising the protease conjugates.

L30 ANSWER 2 OF 5 REGISTRY COPYRIGHT 2001 ACS
RN 266317-46-8 REGISTRY
CN Poly(oxy-1,2-ethanediyl), .alpha.-[[[1-[(butylamino)carbonyl]-5-(carboxyamino)pentyl]amino]carbonyl]-.omega.-methoxy-, ester with .alpha.-hydro-.omega.-hydroxypoly(oxy-1,2-ethanediyl) (2:1) (9CI) (CA INDEX NAME)
MF (C2 H4 O)n (C2 H4 O)n (C2 H4 O)n C26 H48 N6 O9
CI PMS
PCT Polyether
SR CAS Registry Services

PAGE 1-A

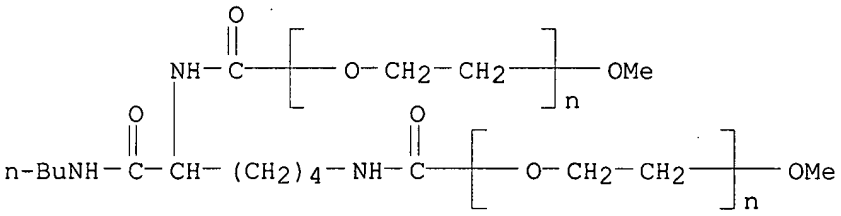


PAGE 1-B

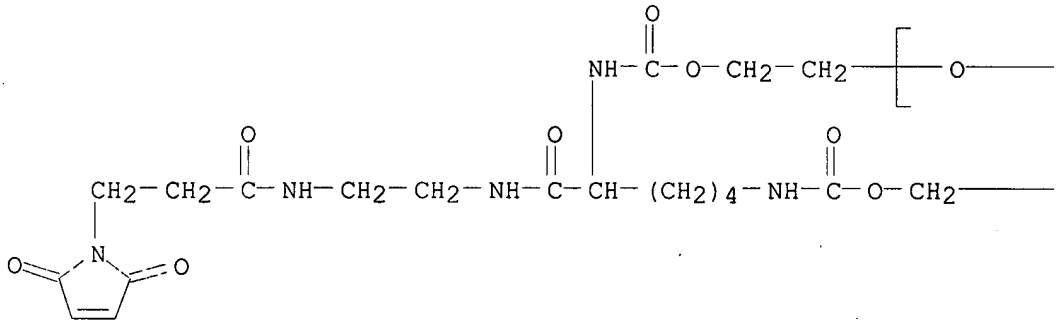


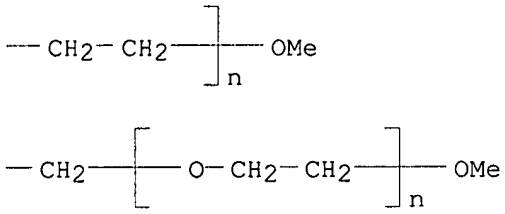
L30 ANSWER 3 OF 5 REGISTRY COPYRIGHT 2001 ACS
RN 266316-83-0 REGISTRY

CN Poly(oxy-1,2-ethanediyl),
.alpha.,.alpha.'-[[1-[(butylamino)carbonyl]-1,5-
pentanediyl]bis(iminocarbonyl)]bis[.omega.-methoxy- (9CI) (CA INDEX
NAME)
MF (C2 H4 O)n (C2 H4 O)n C14 H27 N3 O5
CI PMS
PCT Polyether
SR CAS Registry Services



L30 ANSWER 4 OF 5 REGISTRY COPYRIGHT 2001 ACS
RN 244287-86-3 REGISTRY
CN Poly(oxy-1,2-ethanediyl),
.alpha.,.alpha.'-[[(1S)-1-[[[2-[[3-(2,5-dihydro-
2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]amino]ethyl]amino]carbonyl]-1,5-
pentanediyl]bis(iminocarbonyloxy-2,1-ethanediyl)]bis[.omega.-methoxy-
(9CI) (CA INDEX NAME)
MF (C2 H4 O)n (C2 H4 O)n C23 H37 N5 O10
CI PMS
PCT Polyether
SR CA
LC STN Files: CA, CAPLUS





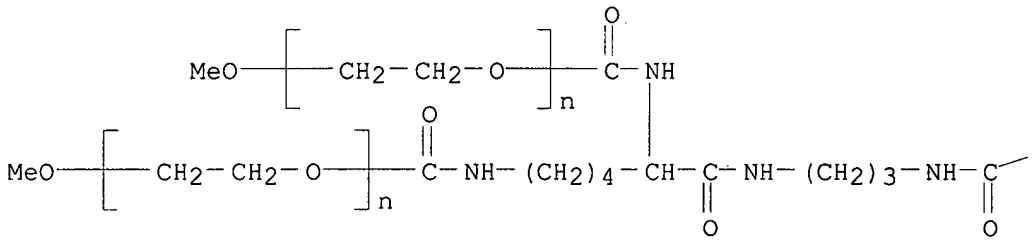
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:254330 Protease conjugates with reduced immunogenicity for cleaning and personal care compositions. Weisberger, David John; Rubingh, Donn Nelton; Correa, Paul Elliott (The Procter & Gamble Company, USA). PCT Int. Appl. WO 9948918 A1 19990930, 45 pp. DESIGNATED STATES: W: AU, BR, CA, CN, CZ, CZ, JP, KR, MX; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1999-IB511 19990325. PRIORITY: US 1998-48174 19980326; US 1998-88912 19980602.

AB The present invention relates to subtilisin protease conjugates comprising a protease moiety and one or more addn. moieties wherein the protease moiety has a modified amino acid sequence of a parent amino acid sequence. The parent amino acid sequence comprises a first epitope region, a second epitope region, and a third epitope region, wherein the modified amino acid sequence comprises a substitution by a substituting amino acid at one or more positions in one or more of the epitope regions and wherein each addn. moiety is covalently attached to one of the substituting moieties. Thus, prominent epitope regions at amino acid positions 70-84, 103-126, and 217-252 in subtilisin BPN' may be substituted and/or chem. modified to alleviate the immunogenic properties of the protease. A variant of subtilisin BPN' with a substitution of leucine for tyrosine at position 217 and a substitution of cysteine for serine at position 78 is conjugated at the cysteine-SH with monomethyl (or dimethyl) polyethylene glycol maleimide. Similarly, succinimide-protected polymer may be coupled selectively to lysine in one or more of the epitope regions. Such subtilisin-like proteases evoke a decreased immunogenic response yet maintain their activity as an efficient and active proteases. The present invention further relates to cleaning and personal care compns. comprising such protease conjugates.

L30 ANSWER 5 OF 5 REGISTRY COPYRIGHT 2001 ACS
RN 204184-14-5 REGISTRY
CN Poly(oxy-1,2-ethanediyl), .alpha.,.alpha.'-[[[1-[[3-[[[2-[7-[1,3-dihydro-3,3-dimethyl-1-(4-sulfobutyl)-2H-indol-2-ylidene]-1,3,5-heptatrienyl]-3,3-dimethyl-1-(4-sulfobutyl)-3H-indolium-5-yl]carbonyl]amino]propyl]amino]carbonyl]-1,5-pentanediyl]bis(iminocarbonyl)]bis[.omega.-methoxy-, inner salt, monosodium salt (9CI) (CA INDEX NAME)
MF (C2 H4 O)n (C2 H4 O)n C49 H68 N6 O12 S2 . Na
CI PMS
PCT Polyether
SR CA
LC STN Files: CA, CAPLUS

PAGE 1-A



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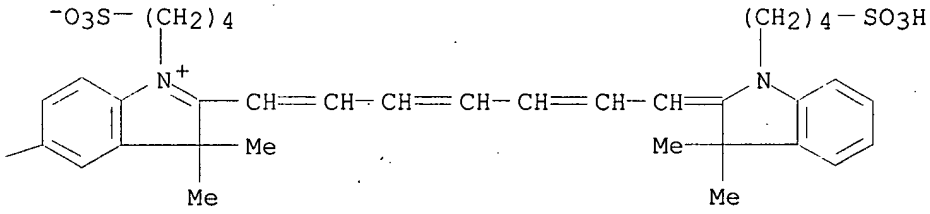
PAGE 1-B



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 128:218365 Synthesis and characterization of cyanine dye - poly(ethylene glycol) conjugates as contrast agents for in vivo fluorescence imaging. Licha, Kai; Riefke, Bjorn; Semmler, Wolfhard (Institut fur Diagnostikforschung GmbH an der Freien Universitat Berlin, Berlin, D-14050, Germany). Proc. SPIE-Int. Soc. Opt. Eng., 3196(Optical and Imaging Techniques for Biomonitoring III), 98-102 (English) 1998. CODEN: PSISDG. ISSN: 0277-786X. Publisher: SPIE-The International Society for Optical Engineering.

AB Cyanine dyes are promising near-IR contrast agents because of their high molar absorption between 700 and 1000 nm, minimal phototoxicity, and convenient synthetic availability. It is known that the derivatization of drugs or contrast agents with polyethylene glycol residues leads to enhanced retention in tumor tissue. The purpose of this study was to generate derivs. of an indotricarbocyanine dye with improved pharmacol. properties enabling in vivo fluorescence detection of tumors. Several hydrophilic indotricarbocyanine-polyethylene glycol conjugates of different mol. wt. were synthesized and characterized physicochem. (partition coeffs., mass distribution) and photophys. (absorption and fluorescence properties in physiol. media) in order to test their applicability as near IR contrast media.

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=> file medl,caplus,biosis,embase,wpids,scisearch,jicst
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                               147.58    1425.36

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)    SINCE FILE      TOTAL
                                                   ENTRY    SESSION
CA SUBSCRIBER PRICE                                -1.68     -17.47

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'IN' IS NOT A VALID FIELD CODE
L31             0 FILE MEDLINE
L32             2 FILE CAPLUS
L33             1 FILE BIOSIS
'IN' IS NOT A VALID FIELD CODE
L34             0 FILE EMBASE
L35             0 FILE WPIDS
'IN' IS NOT A VALID FIELD CODE
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L36 0 FILE SCISEARCH
L37 0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L38 3 ZAHM F?/AU,IN AND HEPATITIS C INFECT?

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PROCESSING COMPLETED FOR L38
L39 3 DUP REM L38 (0 DUPLICATES REMOVED)

=> d 1-3 cbib abs

L39 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2001 ACS
1999:795668 Document No. 132:30856 Use of PEG-IFN-alpha and ribavirin for the treatment of chronic hepatitis. **Zahm, Friederike** (F. Hoffmann-La Roche A.-G., Switz.). PCT Int. Appl. WO 9964016 A1 19991216, 15 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-EP3746 19990529. PRIORITY: EP 1998-110433 19980608.
AB The present invention provides the use of PEG-IFN-.alpha. conjugates in assocn. with Ribavirin for the manuf. of medicaments for the treatment of chronic **hepatitis C infections**. The present invention also provides a method for treating chronic **hepatitis C infections** in patients in need of such treating comprising administering an amt. of PEG-IFN-.alpha. conjugate in assocn. with an amt. of ribavirin effective to treat hepatitis C.

L39 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2001 ACS
1999:219998 Document No. 130:218268 Use of interferon-.alpha. (IFN-.alpha.) and amantadine for the treatment of chronic hepatitis C. **Zahm, Friederike** (F. Hoffmann-La Roche A.-G., Switz.). PCT Int. Appl. WO 9913894 A2 19990325, 11 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-EP5797 19980911.
AB The invention provides the use of IFN-.alpha. in assocn. with amantadine for the manuf. of medicaments for the treatment of chronic **hepatitis C infections**. The invention also provides medicaments contg. the IFN-.alpha. and amantadine as a combined prepn. for simultaneous, sep. or sequential use in therapy of chronic **hepatitis C infections**. The invention further provides a method for treating chronic **hepatitis C infections** in patients in need of such treatment comprising administering an amt. of IFN-.alpha. in assocn. with an amt. of amantadine

effective to treat hepatitis C.

L39 ANSWER 3 OF 3 BIOSIS COPYRIGHT 2001 BIOSIS
1999:434997 Document No.: PREV199900434997. Chronic hepatitis C: Interferon retreatment of relapsers. A meta-analysis of individual patient data. Camma, Calogero (1); Giunta, Marco; Chemello, Liliana; Alberti, Alfredo; Toyoda, Hidenori; Trepo, Christian; Marcellin, Patrick; **Zahm, Friederike**; Schalm, Solko; Craxi, Antonio. (1) Piazza della Cliniche 2, Clinica Medica I, 90100, Palermo Italy. Hepatology, (Sept., 1999) Vol. 30, No. 3, pp. 801-807. ISSN: 0270-9139. Language: English. Summary Language: English.
AB Relapse after interferon (IFN) therapy for chronic hepatitis C virus (HCV) infection occurs in 50% of patients after the initial response. The benefit of retreatment with IFN alone has not been assessed in large controlled studies. To assess the effectiveness and the tolerability of IFN retreatment and to identify the optimal second course regimen, we performed a meta-analysis of individual patient's data on a set of 549 patients (mean age 43.8 years; 12.2 SD, men: 65%) who had an end-of-treatment biochemical response to a first IFN course and then relapsed. Retreatment was started within 24 months after the end of the first course. Biochemical end-of-treatment responses (ETR) and sustained responses (SR) were observed in 405 of 549 (73.8%; 95% confidence interval (CI) 70.1-77.5) and in 124 of 549 (22.6%; CI 19.1-26.1) patients, respectively. One hundred seventy-five of 404 patients (43.3%; CI 38.6-48.2) developed an end-of-treatment, biochemical, and virological response when retreated. A biochemical and virological SR to retreatment occurred in 73 of 494 (14.8%; CI 11.7-18) patients. Thirty-two patients (5.8%; CI 3.5-7.8) stopped retreatment for adverse effects. Biochemical and virological SR was predicted independently by logistic regression analysis using a negative HCV RNA at the end of the first cycle of IFN (P = .01) and by retreatment with a high IFN dose (P = .03). Age, cirrhosis, genotype, and gamma-glutamyl transferase levels before retreatment were not significant by multivariate analysis. The excellent tolerability of IFN monotherapy retreatment makes it an option for patients who transiently cleared HCV-RNA during their first IFN course. Patients should be retreated with a high IFN dose regardless of the strength of the dose received during the previous course of treatment.

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	20.93	1446.29

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-1.18	-18.65

10/037,064

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FILE LAST UPDATED: 23 Nov 2000 (20001123/ED)

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L4	9	SEA FILE=REGISTRY ABB=ON PLU=ON IFN.ALPHA./BI
L5	262	SEA FILE=REGISTRY ABB=ON PLU=ON L4 OR INTERFERON .ALPHA.?/CN
L6	18	SEA FILE=REGISTRY ABB=ON PLU=ON RIBAVIRIN?
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L11 ANSWER 1 OF 10 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 2000:790325 HCAPLUS
TITLE: **PEGylated interferon-.**
alpha.-CCR5 antagonist combination HIV therapy
INVENTOR(S): Laughlin, Mark A.
PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: PCT Int. Appl., 80 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000066141	A2	20001109	WO 2000-US11634	20000501

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-304897 19990504

AB The invention discloses the use of a **PEGylated interferon-.alpha.** and a CCR5 antagonist, further in assocn. with at least one of **ribavirin**, IL-2, IL-12, pentafuside alone or in combination with an anti-HIV-1 drug therapy, e.g., HAART (highly active antiretroviral therapy), for prepn. of a medicament for the treatment of HIV-1 infections as well as HIV-1 infections and HCV co-infections in treatment-naive as well as treatment-experienced adult and pediatric patients.

IT **25322-68-3D, PEG, interferon .alpha.** conjugates **36791-04-5, Ribavirin**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**PEGylated interferon-.alpha.**-CCR5 antagonist combination HIV therapy)

L11 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 2000:755216 HCAPLUS
DOCUMENT NUMBER: 133:317537
TITLE: Hepatitis C virus (HCV) combination therapy, containing **ribavirin** in association with antioxidants
INVENTOR(S): Brass, Clifford A.; Glue, Paul W.; Piken, Edward
PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1046399	A1	20001025	EP 2000-303246	20000418

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WO 2000062799	A1	20001026	WO 2000-US10240	20000418

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RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-294687 19990419

AB Methods are disclosed for treating patients having susceptible viral infections, esp. chronic hepatitis C infection, by administering to the patient a therapeutically effective amt. of a combination therapy of interferon-.alpha. and **ribavirin** for a time sufficient to lower HCV-RNA in assocn. with a therapeutically effective amt. of an antioxidant

for a time sufficient to ameliorate **ribavirin**-related hemolysis.

IT **36791-04-5, Ribavirin**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hepatitis C virus combination therapy contg. interferon .alpha. and **ribavirin** in assocn. with antioxidant)

REFERENCE COUNT: 2
REFERENCE(S):
(1) Brass; GASTROENTEROLOGY, PART 2, DIGESTIVE DISEASE WEEK AND THE 100TH ANNUAL MEETING OF THE AMERICAN GASTROENTEROLOGICAL ASSOCIATION ORLANDO 1999, V116(4), PA1192
(2) Najarian, T; WO 9819670 A 1998

L11 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 2000:628016 HCAPLUS
DOCUMENT NUMBER: 133:206775
TITLE: HIV therapy using pegylated interferon-alfa alone and in assocn. with anti-HIV-1 drug therapy
INVENTOR(S): Laughlin, Mark A.; Glue, Paul W.; Stalgis, Carlos O.
PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000051631	A2	20000908	WO 2000-US5361	20000301
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RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
JP 2000256211	A2	20000919	JP 2000-55695	20000301
EP 1034790	A2	20000913	EP 2000-301695	20000302
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.:
US 1999-260388 19990302
US 1999-268521 19990312
US 1999-288358 19990408
US 1999-454004 19991203

AB The uses of pegylated interferon-alfa, alone, and in assocn. with an anti-HIV-1 drug therapy, and **ribavirin** for the prepn. of a medicament for treating treatment-naive as well as treatment-experienced adult and pediatric patients having HIV-1 infections as well as patients co-infected with HIV-1 and hepatitis C virus (HCV) involving comprising a therapeutically effective amt. of pegylated interferon-alfa, e.g., pegylated interferon alfa-2b as monotherapy or preferably in assocn. with a therapeutically effective amt. of at least one of **ribavirin**, IL-2, IL-12, pentafuside alone or in combination with a therapeutically effective amt. of an anti-HIV-1 drug therapy, e.g., HAART are disclosed.

IT **36791-04-5, Ribavirin 77907-69-8D,**
Interferon-alfa 2a, **pegylated 98530-12-2D,**
Interferon-alfa 2b, **pegylated**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HIV-1 therapy using **pegylated** interferon-alfa alone and in assocn. with anti-HIV-1 drug therapy in relation to hepatitis C virus therapy)

L11 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 2000:517041 HCAPLUS
DOCUMENT NUMBER: 133:260951
TITLE: Firstline treatment for hepatitis C: Combination interferon/**ribavirin** versus interferon monotherapy
AUTHOR(S): Lai, Ming-Yang
CORPORATE SOURCE: Graduate Institute of Clinical Medicine, National Taiwan University College of Medicine, Taipei, Taiwan
SOURCE: J. Gastroenterol. Hepatol. (2000), 15(Suppl.), E130-E133
CODEN: JGHEEO; ISSN: 0815-9319
PUBLISHER: Blackwell Science Asia Pty Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 26 refs. In the initial treatment of chronic hepatitis C, **interferon**-alfa (**IFN-.alpha.**) monotherapy for 24-48 wk induces sustained response rates of only 10-20%. Combination therapy with **IFN-.alpha.** plus **ribavirin** induces a sustained response in 40-50% of patients, and can be now recommended as the first-line therapy for chronic hepatitis C. Stopping therapy at week 12 because of persistent viremia is unnecessary with the combination therapy because later clearance of HCV RNA can still occur with a sustained response. Patients with HCV genotype 1 should receive 48 wk of combination therapy, in contrast to 24 wk for patients with genotypes 2 or 3. For patients who cannot tolerate the side effects of **ribavirin**, such as anemia, **IFN-.alpha.** at 3 MU three times weekly for 48 wk is preferred as the initial therapy. The long-acting **pegylated** IFN can be expected to enhance the efficacy of combination therapy in the treatment of chronic hepatitis C and appears to be much more potent as monotherapy. Further studies are needed to improve the current "half-full" status of chronic hepatitis C treatment.
IT **36791-04-5, Ribavirin**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(combination interferon and **ribavirin** vs. interferon monotherapy for hepatitis C)

L11 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 2000:441658 HCAPLUS
DOCUMENT NUMBER: 133:84228
TITLE: **Ribavirin-PEGylated interferon-.alpha.** induction hepatitis C virus combination therapy
INVENTOR(S): Glue, Paul W.; Albrecht, Janice K.
PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000037110	A2	20000629	WO 1999-US27935	19991216
WO 2000037110	A3	20000914		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UZ, VN, YU
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1998-215876 19981218

AB The invention discloses the use of **ribavirin** and **interferon-.alpha.** for the manuf. of pharmaceutical compns. for treating a patient having chronic hepatitis C infection, e.g., a patient having HCV genotype 1, 2 or 3, to eradicate detectable HCV RNA by a method comprising administering an effective amt. of **ribavirin** in assocn. with an effective amt. of **PEGylated interferon-.alpha.**, characterized in that treating patients having chronic hepatitis C infections is effected in two treatment periods: (a) a first treatment period wherein a therapeutically effective amt. of **ribavirin** and a therapeutically effective induction dosing amt. of **PEGylated interferon-.alpha.**, e.g. **PEGylated interferon-.alpha.**2b sufficient to at least substantially lower, and preferably to eradicate, detectable HCV RNA, are administered; and (b) a second treatment period of at least 20-30 wk wherein a therapeutically effective amt. of **ribavirin** and a therapeutically effective amt. of **PEGylated interferon-.alpha.** are administered sufficient to maintain no detectable HCV RNA for at least 20-30 wk are administered after the end of the first treatment period and to maintain no detectable HCV RNA for at least 24 wk after the end of the second treatment period.

IT **25322-68-3D, Polyethylene glycol, interferon-.alpha.** conjugates **36791-04-5, Ribavirin**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**ribavirin-PEGylated interferon-.alpha.** induction hepatitis C virus combination therapy)

L11 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 2000:441644 HCAPLUS
DOCUMENT NUMBER: 133:72952
TITLE: Treatment of hepatitis C virus infections with interleukin-10
INVENTOR(S): Grint, Paul C.; Nelson, David R.; Davis, Gary L.
PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000037096	A2	20000629	WO 1999-US27952	19991220

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1998-218842 19981222
US 1999-293742 19990416
US 1999-425716 19991022

AB The hepatoprotective effect of IL-10 is described, in particular, the use of interleukin-10 in the treatment of liver damage (e.g. fibrosis or cirrhosis) in a difficult-to-treat patient afflicted with chronic hepatitis C virus infection who has failed to respond to, or achieve a sustained virol. response to an anti-HCV therapy (e.g., interferon-.alpha. in combination with **ribavirin**).

IT **25322-68-3D, PEG12000, interferon alpha** conjugate **36791-04-5, Ribavirin**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of hepatitis C virus infections with interleukin-10)

L11 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 2000:383906 HCAPLUS
DOCUMENT NUMBER: 133:22443
TITLE: 17-Ketosteroids and derivatives, metabolites and precursors in the treatment of hepatitis C virus and other togaviruses
INVENTOR(S): Ahlem, Clarence Nathaniel; Frincke, James Martin; Prendergast, Patrick T.
PATENT ASSIGNEE(S): Hollis-Eden Pharmaceuticals, Inc., USA; Colthurst Ltd
SOURCE: PCT Int. Appl., 99 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000032177	A2	20000608	WO 1999-US28082	19991124

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1998-109924 19981124
US 1999-124087 19990311
US 1999-126056 19990323
OTHER SOURCE(S): MARPAT 133:22443
AB The invention provides the use of 17-ketosteroids, as well as derivs., metabolites and precursors of such compds., and their pharmaceutically acceptable salts, in the treatment of prevention of hepatitis C type virus and/or hepatitis G type virus in patients in need of such treatment. In addn., the invention provides methods to treat or prevent togavirus infections, including infections by 1 or more alphaviruses, flaviviruses, such as yellow fever virus, hepatitis C virus and hepatitis G virus, rubella viruses, or pestiviruses, such as bovine virus diarrhea virus. In addn., the invention provides combination therapies including administration of one or more compd. of the present invention, as defined herein, and administration of one or more compd. selected from plasma concn.-enhancing compds., macrophage stimulating factor, oxidn. agents, **ribavirin** and **alpha-interferon**, and/or oxygen ventilation. The compds. of the present invention may also be used to ameliorate or reduce 1 or more symptoms assocd. with a togavirus infection. Two lots of a non-aq. formulation was made at a 16a-bromoepiandrosterone concn. of 50 mg/mL in 25% **polyethylene glycol** 300, 12.5% dehydrated EtOH, 5% benzyl benzoate, and 57.5% propylene glycol.
IT **36791-04-5, Ribavirin**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ketosteroids and metabolites and precursors in the treatment of hepatitis C virus and togaviruses)

L11 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:795668 HCAPLUS
DOCUMENT NUMBER: 132:30856
TITLE: Use of **PEG-IFN-alpha** and **ribavirin** for the treatment of chronic hepatitis
INVENTOR(S): Zahm, Friederike

PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9964016	A1	19991216	WO 1999-EP3746	19990529
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9945033	A1	19991230	AU 1999-45033	19990529
PRIORITY APPLN. INFO.:			EP 1998-110433	19980608
			WO 1999-EP3746	19990529

AB The present invention provides the use of **PEG-IFN-.alpha.** conjugates in assocn. with **Ribavirin** for the manuf. of medicaments for the treatment of chronic hepatitis C infections. The present invention also provides a method for treating chronic hepatitis C infections in patients in need of such treating comprising administering an amt. of **PEG-IFN-.alpha.** conjugate in assocn. with an amt. of **ribavirin** effective to treat hepatitis C.

IT **25322-68-3D, Polyethyleneglycol**, conjugates with **interferon-.alpha. 36791-04-5 98530-12-2**, Intron A **252269-50-4**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of chronic hepatitis C infections with **PEG-interferon-.alpha.** conjugates and **ribavirin** combination)

REFERENCE COUNT: 6
REFERENCE(S):
(1) Enzon Inc; WO 9513090 A 1995
(2) Hoffmann LA Roche; EP 0510356 A 1992
(3) Hoffmann LA Roche; EP 0593868 A 1994
(4) Schering Corp; EP 0707855 A 1996
(5) Schering Corp; WO 9716204 A 1997
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:736231 HCAPLUS
DOCUMENT NUMBER: 131:317758
TITLE: Combination therapy comprising **ribavirin** and interferon-.alpha. in antiviral treatment-naive patients having chronic hepatitis C infection
INVENTOR(S): Albrecht, Janice K.
PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: Eur. Pat. Appl., 26 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 956861	A1	19991117	EP 1999-303729	19990513
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, SI, LT, LV, FI, RO
WO 9959621 A1 19991125 WO 1999-US7037 19990513
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MD, MG, MK, MN, MX, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
AU 9938600 A1 19991206 AU 1999-38600 19990513
PRIORITY APPLN. INFO.: US 1998-79566 19980515
WO 1999-US7037 19990513

AB Use of **ribavirin** and interferon-.alpha. to prep. pharmaceutical compns. for a treating antiviral treatment-naive patient having chronic hepatitis C infection to eradicate detectable HCV RNA involving a combination therapy using a therapeutically effective amt. of **ribavirin** and a therapeutically effective amt. of interferon-.alpha. for a period of from 20 up to 50 wk is disclosed.

IT **25322-68-3D, PEG**, conjugates with **interferon-.alpha.**2a or **interferon-.alpha.**2b
36791-04-5, Ribavirin
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**ribavirin** and **interferon-.alpha.** combination therapy for antiviral treatment-naive patients having chronic hepatitis C infection)

REFERENCE COUNT: 9
REFERENCE(S):
(1) Bizollon, T; HEPATOLOGY 1997, V26(2), P500 HCAPLUS
(2) Braconier, J; SCANDINAVIAN JOURNAL OF INFECTIOUS DISEASES 1995, V27(4), P325 MEDLINE
(3) Chemello, L; JOURNAL OF HEPATOLOGY 1994, V21(Suppl 01), PS12
(4) McHutchison, J; NEW ENGLAND JOURNAL OF MEDICINE 1998, V339(21), P1485 HCAPLUS
(7) Reichard, O; THE LANCET 1998, V351(9096), P83 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:213143 HCAPLUS
DOCUMENT NUMBER: 130:218266
TITLE: Combination therapy with interferon-.alpha. and **ribavirin** for eradicating detectable HCV-RNA in patients having chronic hepatitis C infection
INVENTOR(S): Albrecht, Janice K.
PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: Eur. Pat. Appl., 19 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 903148	A2	19990324	EP 1998-306332	19980807
EP 903148	A3	19990428		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
ZA 9808466	A	19990316	ZA 1998-8466	19980916
WO 9915194	A1	19990401	WO 1998-US18488	19980916
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HR, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9894737	A1	19990412	AU 1998-94737	19980916
BR 9812484	A	20000919	BR 1998-12484	19980916
JP 11152231	A2	19990608	JP 1998-266599	19980921
NO 2000001437	A	20000320	NO 2000-1437	20000320
PRIORITY,APPLN. INFO.:			US 1997-938033	19970921
			US 1997-935123	19970922
			WO 1998-US18488	19980916

AB The use of **ribavirin**, interferon-.alpha. or a combination of **ribavirin** and interferon-.alpha. is disclosed for the manuf. of a pharmaceutical compn. for treating a patient having chronic hepatitis C infection to eradicate detectable HCV-RNA by a method comprising administering an effective amt. of **ribavirin** in assocn. with an effective amt. of interferon-.alpha., wherein the patient is one having failed to respond to a previous course of interferon-.alpha. therapy. The compns. may be used in a method for treating a patient having chronic hepatitis C infection to eradicate detectable HCV-RNA involving a combination therapy using a therapeutically effective amt. of **ribavirin** and a therapeutically effective amt. of interferon-.alpha. for a time period of from 20 up to 80 wk.

IT **25322-68-3D, PEG, interferon-.alpha.** conjugates **36791-04-5, Ribavirin**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**interferon-.alpha.-ribavirin** combination therapy for eradicating detectable HCV-RNA in patients with chronic hepatitis C infection)

=> select hit rn l11 1-10

E1 THROUGH E5 ASSIGNED

=> fil reg

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DICTIONARY FILE UPDATES: 23 NOV 2000 HIGHEST RN 304429-00-3

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Structure search limits have been increased. See HELP SLIMIT for details.

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1 36791-04-5/BI
(36791-04-5/RN)
1 25322-68-3/BI
(25322-68-3/RN)
1 98530-12-2/BI
(98530-12-2/RN)
1 252269-50-4/BI

(252269-50-4/RN)
1 77907-69-8/BI
(77907-69-8/RN)
L12 5 (36791-04-5/BI OR 25322-68-3/BI OR 98530-12-2/BI OR 252269-50-4/BI OR 77907-69-8/BI)

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=> d ide can l12 1-5

L12 ANSWER 1 OF 5 REGISTRY COPYRIGHT 2000 ACS
RN **252269-50-4** REGISTRY
CN Interferon .alpha.2 (human leukocyte clone pM21 protein moiety reduced), mixt. with 1-.beta.-D-ribofuranosyl-1H-1,2,4-triazole-3-carboxamide (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1H-1,2,4-Triazole-3-carboxamide, 1-.beta.-D-ribofuranosyl-, mixt. contg. (9CI)
FS STEREOSEARCH
MF C8 H12 N4 O5 . Unspecified
CI MXS
SR CA
LC STN Files: CA, CAPLUS, TOXLIT

CM 1

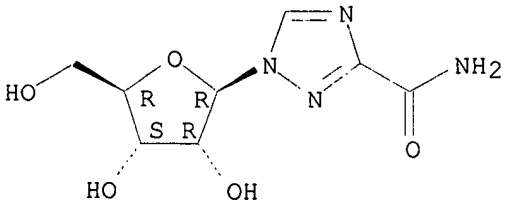
CRN 98530-12-2
CMF Unspecified
CCI MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 2

CRN 36791-04-5
CMF C8 H12 N4 O5

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:30856

L12 ANSWER 2 OF 5 REGISTRY COPYRIGHT 2000 ACS
RN **98530-12-2** REGISTRY
CN Interferon .alpha.2 (human leukocyte clone pM21 protein moiety reduced) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN .alpha.AD-Interferon (human clone 36422.pep)
CN 11: PN: WO0009143 SEQID: 24 claimed protein
CN 7: PN: WO0006735 FIGURE: 5 claimed protein
CN Interferon .alpha.2b (human leukocyte clone Hif-SN206 protein moiety reduced)

CN Interferon .alpha.2b (human)
CN Interferon alfa-2b
CN Interferon-.alpha.2b (plasmid pMON20442)
CN Interferon-.alpha.2b (plasmid pMON30422)
CN Interferon-.alpha.2b (plasmid pMON30426)
CN Intron A
CN PN: WO9951638 SEQID: 19 claimed protein
FS PROTEIN SEQUENCE
DR 99210-65-8
MF Unspecified
CI COM, MAN
SR CA
LC STN Files: ADISINSIGHT, AGRICOLA, AIDSLINE, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CBNB, CEN, CIN, DDFU, DRUGU, EMBASE, IMSDIRECTORY, IPA, MEDLINE, MRCK*, PHAR, PROMT, RTECS*, TOXLINE, TOXLIT, USAN, USPATFULL
(*File contains numerically searchable property data)

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65 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
65 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:265657

REFERENCE 2: 133:265656

REFERENCE 3: 133:206775

REFERENCE 4: 133:175532

REFERENCE 5: 133:16182

REFERENCE 6: 133:13406

REFERENCE 7: 132:333220

REFERENCE 8: 132:307061

REFERENCE 9: 132:264110

REFERENCE 10: 132:264087

L12 ANSWER 3 OF 5 REGISTRY COPYRIGHT 2000 ACS
RN **77907-69-8** REGISTRY
CN Interferon .alpha.A (human leukocyte protein moiety) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Interferon alfa-2a
CN Roferon A
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
LC STN Files: BIOBUSINESS, BIOSIS, CA, CAPLUS, CIN, DRUGNL, DRUGPAT, DRUGUPDATES, IMSDIRECTORY, IPA, MRCK*, PHAR, PROMT, TOXLINE, TOXLIT
(*File contains numerically searchable property data)

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34 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
34 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:295376

REFERENCE 2: 133:265657

REFERENCE 3: 133:265656

REFERENCE 4: 133:251091

REFERENCE 5: 133:206775

REFERENCE 6: 133:175532

REFERENCE 7: 133:172533

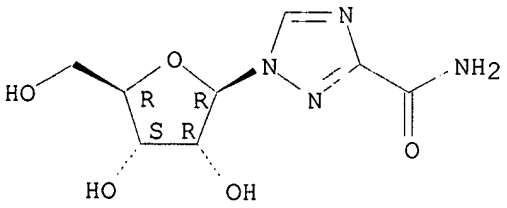
REFERENCE 8: 133:419

REFERENCE 9: 132:206792

REFERENCE 10: 132:164947

L12 ANSWER 4 OF 5 REGISTRY COPYRIGHT 2000 ACS
RN **36791-04-5** REGISTRY
CN 1H-1,2,4-Triazole-3-carboxamide, 1-.beta.-D-ribofuranosyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN ICN 1229
CN NSC 163039
CN Ribamide
CN Ribamidil
CN Ribavirin
CN Tribavirin
CN Vilona
CN Viramid
CN Virazole
FS STEREOSEARCH
DR 66510-90-5
MF C8 H12 N4 O5
CI COM
LC STN Files: AGRICOLA, AIDSLINE, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IMSDIRECTORY, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PHAR, PIRA, PROMT, RTECS*, TOXLINE, TOXLIT, USAN, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: WHO

Absolute stereochemistry.



1084 REFERENCES IN FILE CA (1967 TO DATE)
49 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1085 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:325722

REFERENCE 2: 133:325607

REFERENCE 3: 133:318963

REFERENCE 4: 133:317537

REFERENCE 5: 133:310142

REFERENCE 6: 133:309791

REFERENCE 7: 133:305291

REFERENCE 8: 133:296659

REFERENCE 9: 133:276317

REFERENCE 10: 133:275857

L12 ANSWER 5 OF 5 REGISTRY COPYRIGHT 2000 ACS
RN **25322-68-3** REGISTRY
CN Poly(oxy-1,2-ethanediyl), .alpha.-hydro-.omega.-hydroxy- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN .alpha.,.omega.-Hydroxypoly(ethylene oxide)
CN .alpha.-Hydro-.omega.-hydroxypoly(oxy-1,2-ethanediyl)
CN .alpha.-Hydro-.omega.-hydroxypoly(oxyethylene)
CN 1,2-Ethanediol, homopolymer
CN 1660O
CN 1660S
CN 3: PN: US6077939 SEQID: 3 claimed sequence
CN Alkox
CN Alkox E 100
CN Alkox E 130
CN Alkox E 160
CN Alkox E 240
CN Alkox E 30
CN Alkox E 45
CN Alkox E 60
CN Alkox E 75
CN Alkox R 1000
CN Alkox R 15
CN Alkox R 150
CN Alkox R 400
CN Alkox SR
CN Antarox E 4000
CN Aquacide III
CN Aquaffin
CN Badimol
CN BDH 301
CN Bradsyn PEG
CN Breox 2000
CN Breox 20M
CN Breox 4000
CN Breox 550
CN Breox PEG 300
CN CAFO 154
CN Carbowax
CN Carbowax 100
CN Carbowax 1000
CN Carbowax 1350
CN Carbowax 14000
CN Carbowax 1500
CN Carbowax 1540
CN Carbowax 20
CN Carbowax 200
CN Carbowax 20000
CN Carbowax 25000
CN Carbowax 300

CN Carbowax 3350
CN Carbowax 400
CN Carbowax 4000
CN Carbowax 4500
CN Carbowax 4600
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CI PMS, COM
PCT Polyether
LC STN Files: AGRICOLA, ANABSTR, APILIT, APILIT2, APIPAT, APIPAT2, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CHEMSAFE, CIN, CSCHEM, CSNB, DDFU, DETHERM*, DIOGENES, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PDLCOM*, PIRA, PROMT, RTECS*, SPECINFO, TOXLINE, TOXLIT, TULSA, ULIDAT, USAN, USPATFULL, VETU, VTB
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Other Sources: DSL**, TSCA**, WHO
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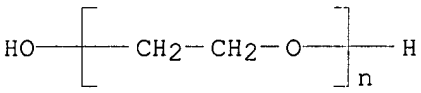

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REFERENCE 1: 133:328447

REFERENCE 2: 133:328307

REFERENCE 3: 133:327703

REFERENCE 4: 133:327593

REFERENCE 5: 133:326968

REFERENCE 6: 133:326112

REFERENCE 7: 133:325952

REFERENCE 8: 133:325706

REFERENCE 9: 133:325684

REFERENCE 10: 133:325682

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FILE LAST UPDATED: 23 Nov 2000  (20001123/ED)

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=> d stat que l13

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L3           896 SEA FILE=REGISTRY ABB=ON  PLU=ON  PEG?
L4             9 SEA FILE=REGISTRY ABB=ON  PLU=ON  IFN.ALPHA./BI
L5           262 SEA FILE=REGISTRY ABB=ON  PLU=ON  L4 OR INTERFERON .ALPHA.?/CN

L6            18 SEA FILE=REGISTRY ABB=ON  PLU=ON  RIBAVIRIN?
L7        358819 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L2 OR L3 OR PEG? OR (POLY(W)ET
                 HYLENE OR POLYETHYLENE)(5A)GLYCOL OR POLYETHYLENEGLYCOL?
L8         16615 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L5 OR (IFN OR INTERFERON)(5A)A
                 LPHA?
L9          1328 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L6 OR RIBAVIRIN?
L10           90 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L7(L)L8
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L13  ANSWER 1 OF 4  HCAPLUS  COPYRIGHT 2000 ACS
ACCESSION NUMBER:         2000:493265  HCAPLUS
DOCUMENT NUMBER:          133:99539
TITLE:                    Antiviral agent-vaccine combination for treatment of
                          hepatitis B virus infection
INVENTOR(S):              Atkinson, Gillian Frances; Boon, Ronald James;
                          Vandepapeliere, Pierre G.; Wettendorff, Martine Anne
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Cecile
PATENT ASSIGNEE(S): SmithKline Beecham Biologicals S.A., Belg.
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000041463	A2	20000720	WO 1999-EP10295	19991221

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 1999-630 19990112

AB The invention provides a pharmaceutical pack comprising as active ingredients (1) an antiviral agent active against hepatitis B virus and (2) a vaccine for the prophylaxis and/or treatment of hepatitis B infection, the active ingredients being for simultaneous or sequential use. Preferred components are a nucleoside analog as the antiviral agent, together with a hepatitis B virus vaccine which comprises a hepatitis B virus surface antigen.

IT **36791-04-5**, **Ribavirin**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiviral agent-vaccine combination for treatment of hepatitis B virus infection)

IT **9005-65-6**, Tween 80
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiviral agent-vaccine combination for treatment of hepatitis B virus infection)

L13 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 2000:260065 HCAPLUS
DOCUMENT NUMBER: 132:288757
TITLE: Selective eradication of virally infected cells by combined use of a cytotoxic agent and an antiviral agent
INVENTOR(S): Korant, Bruce D.
PATENT ASSIGNEE(S): Du Pont Pharmaceuticals Company, USA
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000021565	A1	20000420	WO 1999-US23192	19991005

W: AL, AU, BR, CA, CN, CZ, EE, HU, IL, IN, JP, KR, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, VN, ZA
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

AU 9965088	A1	20000501	AU 1999-65088	19991005

PRIORITY APPLN. INFO.: US 1998-103922 19981013
WO 1999-US23192 19991005

AB A method for treating human immunodeficiency virus (HIV) infection in a mammal comprises administering to the mammal a therapeutically effective

amt. of a combination of: (i) at least one cytotoxic agent and (ii) at least one nonnucleoside reverse transcriptase HIV inhibitor. Also provided is a method of treating chronic viral infections comprising administering to the mammal a therapeutically effective amt. of a combination of: (i) at least one cytotoxic agent and (ii) at least one antiviral agent.

IT **36791-04-5D**, Virazole, mixt. with **Interferon .alpha. 130167-69-0, Pegaspargase**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cytotoxic agent-antiviral agent combination for selective eradication of virally infected cells)

REFERENCE COUNT: 1
REFERENCE(S): (1) Merck & Co; EP 0617968 A 1994

L13 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:766507 HCAPLUS
DOCUMENT NUMBER: 130:29221
TITLE: Preparation of solid porous matrixes for pharmaceutical uses
INVENTOR(S): Unger, Evan C.
PATENT ASSIGNEE(S): Imarx Pharmaceutical Corp., USA
SOURCE: PCT Int. Appl., 139 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9851282	A1	19981119	WO 1998-US9570	19980512
W: AU, BR, CA, CN, JP, KR, NZ				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9873787	A1	19981208	AU 1998-73787	19980512
EP 983060	A1	20000308	EP 1998-921109	19980512
R: DE, FR, GB, IT, NL				
PRIORITY APPLN. INFO.:			US 1997-46379	19970513
			US 1998-75477	19980511
			WO 1998-US9570	19980512

AB A solid porous matrix formed from a surfactant, a solvent, and a bioactive agent is described. Thus, amphotericin nanoparticles were prepd. by using ZrO2 beads and a surfactant. The mixt. was milled for 24 h.

IT **9003-11-6 9005-64-5**, Polyoxyethylene sorbitan monolaurate **9005-65-6**, Polyoxyethylene sorbitan monooleate **9005-66-7**, Polyoxyethylene sorbitan monopalmitate **9005-67-8**, Polyoxyethylene sorbitan monostearate **9005-71-4**, Polyoxyethylene sorbitan tristearate **9036-19-5**, Octoxynol **25322-68-3 25322-68-3D, PEG**, ethers **36791-04-5, Ribavirin**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of solid porous matrixes for pharmaceutical uses)

REFERENCE COUNT: 1
REFERENCE(S): (1) Wong; US 5569448 A 1996

L13 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1993:154600 HCAPLUS
DOCUMENT NUMBER: 118:154600
TITLE: Antiviral pharmaceutical compositions for vaginal administration
INVENTOR(S): Conte, Ubaldo; Maggi, Lauretta
PATENT ASSIGNEE(S): L.C. Pharchem Ltd., Cyprus
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9302662	A1	19930218	WO 1992-EP1655	19920720
W: AU, BB, BG, BR, CA, CS, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, PL, RO, RU, SD, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
CA 2114216	AA	19930218	CA 1992-2114216	19920720
AU 9223454	A1	19930302	AU 1992-23454	19920720
EP 596935	A1	19940518	EP 1992-915980	19920720
EP 596935	B1	19951018		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE				
JP 06509348	T2	19941020	JP 1992-503217	19920720
AT 129149	E	19951115	AT 1992-915980	19920720
CN 1082894	A	19940302	CN 1992-111077	19920824
PRIORITY APPLN. INFO.:			IT 1991-MI2071	19910726
			WO 1992-EP1655	19920720

AB The title compns. in the form of sustained-release tablets comprise virucides and biocompatible bioadhesive polymers. For example, a tablet contained acyclovir 200, hydroxypropyl Me cellulose 200, mannitol 400, maize starch 400, adipic acid 70, talc 20, and Mg stearate 10 mg.

IT **36791-04-5**
RL: BIOL (Biological study)
(sustained-release compns. contg., for vaginal administration)

IT **25322-68-3, Polyethylene glycol**
RL: BIOL (Biological study)
(virucidal sustained-release compns. contg., for vaginal administration)

=> select hit rn l13 1-4

E6 THROUGH E15 ASSIGNED

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DICTIONARY FILE UPDATES: 23 NOV 2000 HIGHEST RN 304429-00-3

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Structure search limits have been increased. See HELP SLIMIT for details.

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                (9005-65-6/RN)
              1 130167-69-0/BI
                (130167-69-0/RN)
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                (9003-11-6/RN)
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                I OR 9005-71-4/BI OR 9036-19-5/BI) NOT L12

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L14  ANSWER 1 OF 8  REGISTRY  COPYRIGHT 2000 ACS
RN   130167-69-0  REGISTRY
CN   Pegaspargase (9CI)  (CA INDEX NAME)
MF   Unspecified
CI   MAN
SR   US Adopted Names Council
LC   STN Files:   ADISINSIGHT, BIOBUSINESS, BIOSIS, CA, CAPLUS, CIN, DRUGNL,
       DRUGPAT, DRUGUPDATES, IPA, MRCK*, PROMT, TOXLINE, TOXLIT, USAN
         (*File contains numerically searchable property data)

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REFERENCE   2:  130:119591

REFERENCE   3:  129:169941

REFERENCE   4:  129:156545

REFERENCE   5:  127:12853

L14  ANSWER 2 OF 8  REGISTRY  COPYRIGHT 2000 ACS
RN   9036-19-5  REGISTRY
CN   Poly(oxy-1,2-ethanediyl), .alpha.-[(1,1,3,3-tetramethylbutyl)phenyl]-
     .omega.-hydroxy- (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   Glycols, polyethylene, mono[(1,1,3,3-tetramethylbutyl)phenyl] ether (8CI)
OTHER NAMES:
CN   Alkasurf OP
CN   Alkasurf OP 10
CN   Alkasurf OP 12
CN   Alkasurf OP 30
CN   Alkasurf OP 40
CN   Alkasurf OP 5
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CN Alkasurf OP 8
CN Antarox CA 420
CN Antarox CA 520
CN Antarox CA 620
CN Antarox CA 897
CN Cemulsol OP 16
CN Cemulsol P 9
CN Charger E
CN Delonic OPE 10
CN Disponil A 4065EXP
CN Emulgen 808
CN Emulgen 810
CN Emulgen 810S
CN Emulgen 840S
CN Emulsifier OP
CN EP 680
CN Ethoxylated octylphenol
CN Ethylan CP
CN Ethylan CPX
CN HS 2045
CN HS 208
CN HS 215
CN Hydrol
CN Hydrol (surfactant)
CN Hyonic OP 9
CN Hyonic PE 260
CN Igepal CA
CN Igepal CA 210
CN Igepal CA 300
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CN Igepal CA 630
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CN Igepal CA 877
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CN Invadin JFC 800
CN Macol OP 10SP
CN Macol OP 5
CN Marlophen 84
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MF (C2 H4 O)n C14 H22 O
CI IDS, PMS, COM
PCT Polyether
LC STN Files: AGRICOLA, AIDSLINE, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DETHERM*, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MSDS-OHS, NIOSHTIC, PIRA, PROMT, RTECS*, TOXLINE, TOXLIT, USPATFULL
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Other Sources: DSL**, TSCA**
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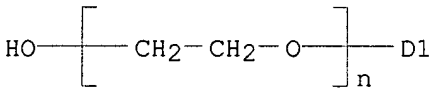

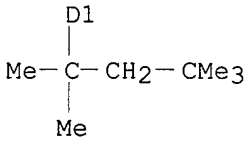

2939 REFERENCES IN FILE CA (1967 TO DATE)
61 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2943 REFERENCES IN FILE CAPLUS (1967 TO DATE)

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REFERENCE 2: 133:323298

REFERENCE 3: 133:322393

REFERENCE 4: 133:310933

REFERENCE 5: 133:310871

REFERENCE 6: 133:286400

REFERENCE 7: 133:280644

REFERENCE 8: 133:280549

REFERENCE 9: 133:278221

REFERENCE 10: 133:270289

L14 ANSWER 3 OF 8 REGISTRY COPYRIGHT 2000 ACS
RN **9005-71-4** REGISTRY
CN Sorbitan, trioctadecanoate, poly(oxy-1,2-ethanediyl) derivs. (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Sorbitan, tristearate, polyoxyethylene derivs. (8CI)
OTHER NAMES:
CN Ahco 7166T
CN Emsorb 6907
CN Ethoxylated sorbitan tristearate
CN Glycosperse TS 20
CN Liposorb TS 20
CN Montanox 65
CN Nikkol TS 30
CN Poly(oxyethylene) sorbitan tristearate
CN Polyethylene glycol sorbitan ether tristearate
CN Polyethylene glycol sorbitan tristearate
CN Polyethylene glycol sorbitan tristearate ether
CN Polyoxyethylene 20 sorbitan tristearate
CN Polysorbate 65
CN Rheodol TW-S 320
CN Sorbimacrogol tristearate 300
CN T-MAZ 65K

CN Tween 65
DR 9015-61-6
MF Unspecified
CI PMS, COM, MAN
PCT Manual registration
LC STN Files: ANABSTR, BIOBUSINESS, BIOSIS, CA, CAPLUS, CHEMCATS, CHEMLIST, CIN, CSCHEM, CSNB, EMBASE, IFICDB, IFIPAT, IFIUDB, PIRA, RTECS*, TOXLINE, TOXLIT, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, TSCA**
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315 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
315 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:323314

REFERENCE 2: 133:298640

REFERENCE 3: 133:198412

REFERENCE 4: 133:168183

REFERENCE 5: 133:155507

REFERENCE 6: 133:155314

REFERENCE 7: 133:154974

REFERENCE 8: 133:139506

REFERENCE 9: 133:60459

REFERENCE 10: 133:48691

L14 ANSWER 4 OF 8 REGISTRY COPYRIGHT 2000 ACS
RN **9005-67-8** REGISTRY
CN Sorbitan, monooctadecanoate, poly(oxy-1,2-ethanediyl) derivs. (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Ahco DFS 100
CN Ahco DFS 149
CN Armotan PMS 20
CN Atlas G 1036
CN Crill 8
CN Crill 9
CN Crill S 8
CN Crillet 3
CN Crillet 31
CN Disponil SMS 120F1
CN Drewpone 60
CN Durfax 60K
CN Emasol 3130
CN Emerest 2654
CN Emsorb 6905
CN Emsorb 6906
CN Emulgin SMS 20
CN Ethoxylated sorbitan monostearate
CN Eumulgin SMS 20
CN Glycosperse S 20
CN Montanox 60
CN Montanox 60DF
CN MS 55F
CN Newcol 65

CN Nikkol TS 10
CN Nikkol TS 106
CN Nissan Nonion ST 202
CN Nissan Nonion ST 221
CN Nissan Nonion STN 201.5
CN Nonio-light TWS 13
CN Nonion ST 221
CN Polisorbac 80
CN Poly(oxyethylene) sorbitol monostearate
CN Poly(oxyethylene)sorbitan monostearate
CN Polyethylene glycol sorbitan monostearate
CN Polyethylene glycol sorbitan monostearate ether
CN Polyethylene sorbitan monostearate
CN Polyoxyethylene sorbitan monooctadecanoate
CN Polyoxyethylene sorbitan monostearic acid ester
CN Polyoxyethylene sorbitan stearate
CN Polysorbate 60
CN Polysorbate 61
CN Rheodol Super TW-S 120
CN Rheodol TW-S 106
CN Rheodol TW-S 120
CN Rokwinol 60
CN Silvan T 60
CN Sorbimacrogol stearate 300
CN Sorbital S 20
CN Sorbitan monostearate polyethylene glycol ether
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for DISPLAY
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MF Unspecified
CI PMS, COM, MAN
PCT Manual registration, Polyether
LC STN Files: AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CBNB, CHEMCATS, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MSDS-OHS, NIOSHTIC, PIRA, PROMT, RTECS*, TOXLINE, TOXLIT, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
2256 REFERENCES IN FILE CA (1967 TO DATE)
15 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2258 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:325661

REFERENCE 2: 133:314082

REFERENCE 3: 133:310679

REFERENCE 4: 133:301171

REFERENCE 5: 133:300746

REFERENCE 6: 133:298640

REFERENCE 7: 133:282998

REFERENCE 8: 133:260604

REFERENCE 9: 133:257493

REFERENCE 10: 133:256796

L14 ANSWER 5 OF 8 REGISTRY COPYRIGHT 2000 ACS
RN **9005-66-7** REGISTRY
CN Sorbitan, monohexadecanoate, poly(oxy-1,2-ethanediyl) derivs. (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Sorbitan, monopalmitate, polyoxyethylene derivs. (8CI)
OTHER NAMES:
CN Crill 7
CN Crillet 2
CN Durfax 60
CN Emsorb 6910
CN Emulgen TWP 120
CN Ethoxylated sorbitan monopalmitate
CN Glycosperse P 20
CN Lonzest SMP 20
CN Montanox 40
CN MP 55F
CN Nikkol TP 10
CN Nissan Nonion PT 221
CN Polyethylene glycol sorbitan monohexadecanoate
CN Polyethylene glycol sorbitan monopalmitate
CN Polyethylene glycol-sorbitan monopalmitate adduct
CN Polyethylene sorbitan monopalmitate
CN Polyoxyethylene sorbitan monohexadecanoate
CN Polyoxyethylene sorbitan monopalmitate
CN Polysorbate 40
CN Rheodol TW-P 120
CN Sorbimacrogol palmitate 300
CN Sorbitan monopalmitate polyethylene glycol ether
CN Sorbitan polyethoxy monopalmitate
CN Sorbon T 40
CN Tween 16:0
CN Tween 40
DR 9015-58-1, 1340-84-7, 118955-40-1
MF Unspecified
CI PMS, COM, MAN
PCT Manual registration
LC STN Files: AGRICOLA, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CHEMCATS, CHEMLIST, CIN, CSCHEM, CSNB, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MSDS-OHS, NIOSHTIC, PROMT, RTECS*, TOXLINE, TOXLIT, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
1188 REFERENCES IN FILE CA (1967 TO DATE)
7 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1188 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:323314

REFERENCE 2: 133:305106

REFERENCE 3: 133:301171

REFERENCE 4: 133:282998

REFERENCE 5: 133:282490

REFERENCE 6: 133:275628

REFERENCE 7: 133:270491

REFERENCE 8: 133:257493

REFERENCE 9: 133:213178

REFERENCE 10: 133:213151

L14 ANSWER 6 OF 8 REGISTRY COPYRIGHT 2000 ACS
RN **9005-65-6** REGISTRY
CN Sorbitan, mono-(9Z)-9-octadecenoate, poly(oxy-1,2-ethanediyl) derivs. (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Glycols, polyethylene, ether with sorbitan monooleate (8CI)
OTHER NAMES:
CN Alkamuls PSMO 20
CN Atlox 1087
CN Atlox 8916TF
CN Capmul POE-O
CN Cemerol T 80
CN Cemesol TW 1020
CN Crill 10
CN Crill 11
CN Crill S 10
CN Crillet 4
CN Crillet 4 Super
CN Crillet 41
CN Disponil SMO 120
CN Durfax 80
CN Emasol O 105R
CN Emsorb 6900
CN Emulson 10OM
CN Ethoxylated sorbitan monooleate
CN Ethylene oxide-sorbitan monooleate polymer
CN Eumulgin SMO 20
CN Flo Mo SMO 20
CN Glycosperse O 20
CN Glycosperse O 5
CN Hexaethylene glycol sorbitan monooleate
CN Hodag SVO 9
CN Ionet T 80
CN Ionet T 80C
CN MO 55F
CN Monitan
CN Montanox 80
CN Myvatex MSPS
CN Nikkol TO 10
CN Nikkol TO 106
CN Nikkol TO 10M
CN Nissan Nonion OT 221
CN Nonion OT 221
CN Olothorb
CN Polisorbac 60
CN Polyethoxylated sorbitan monooleate
CN Polyethylene glycol sorbitan ether monooleate
CN Polyethylene glycol sorbitan monooleate
CN Polyoxyethylated sorbitan monooleate
CN Polyoxyethylene monosorbitan monooleate
CN Polyoxyethylene sorbitan monooleate
CN Polyoxyethylenesorbitan oleate
CN Polysorban 80
CN Polysorbate 80
CN Polysorbate 81
CN Radiasurf 7157
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for DISPLAY
DR 8050-83-7, 9015-07-0, 9050-49-1, 9050-57-1, 1340-85-8, 51377-27-6, 61723-75-9, 37199-23-8, 37280-84-5, 141927-23-3, 178631-96-4
MF Unspecified
CI PMS, COM, MAN

PCT Manual registration, Polyether
LC STN Files: AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DIOGENES, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MRCK*, MSDS-OHS, NIOSHTIC, PDLCOM*, PIRA, PROMT, RTECS*, TOXLINE, TOXLIT, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
6826 REFERENCES IN FILE CA (1967 TO DATE)
40 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
6832 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:328974

REFERENCE 2: 133:323314

REFERENCE 3: 133:321043

REFERENCE 4: 133:316429

REFERENCE 5: 133:313641

REFERENCE 6: 133:313639

REFERENCE 7: 133:313636

REFERENCE 8: 133:313600

REFERENCE 9: 133:305106

REFERENCE 10: 133:305032

L14 ANSWER 7 OF 8 REGISTRY COPYRIGHT 2000 ACS
RN **9005-64-5** REGISTRY
CN Sorbitan, monododecanoate, poly(oxy-1,2-ethanediyl) derivs. (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Ahco 7596T
CN Alkamuls PSML 20
CN Armotan PML 20
CN Atlas G 4280
CN Atlas G 7596J
CN Atlas G 7596P
CN Atmer 110
CN Crillet 1
CN Disponil SML 120
CN Emasol 1112
CN Emasol L 130
CN Emsorb 6915
CN Ethoxylated sorbitan monolaurate
CN Ethylene oxide-sorbitan monolaurate adduct
CN Ethylene oxide-sorbitan monolaurate polymer
CN Eumulgin SML 20
CN G 1020
CN G 4280
CN G 7596J
CN G 7606J
CN GL 1
CN GL 1 (carbohydrate)
CN Glytanox 1001
CN Ionet T 20C
CN Kemotan T 20
CN LT 221

CN ML 55F
CN Montanox 20
CN Nikkol TL 10
CN Nissan Nonion LT 221
CN Nonion LT 221
CN Oxyethylated sorbitan monolaurate
CN Oxysorbic 20
CN Poly(ethylene glycol) sorbitan ether monolaurate
CN Poly(oxyethylene sorbitan laurate)
CN Poly(oxyethylene)sorbitan ether monolaurate
CN Poly(oxyethylene)sorbitan monolaurate
CN Polyethylene glycol sorbitan monolaurate
CN Polyoxethylene sorbitan monolaurate
CN Polyoxyethylene sorbitan monododecanoate
CN Polyoxyethylene Span 20
CN Polysorbate 20
CN Polysorbate 21
CN Polysten 20
CN Radiasurf 7137
CN Rheodol Super TW-L 120
CN Rheodol Super TW-L 20
CN Rheodol TW-L 100
CN Rheodol TW-L 106
CN Rheodol TW-L 120
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for DISPLAY
DR 8036-82-6, 9011-30-7, 9015-57-0, 1341-06-6, 122304-31-8, 54174-54-8, 60318-54-9, 129428-64-4, 62229-28-1, 118955-39-8, 37310-96-6, 93037-36-6, 194879-92-0
MF Unspecified
CI PMS, COM, MAN
PCT Manual registration, Polyether
LC STN Files: AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MSDS-OHS, NIOSHTIC, PDLCOM*, PIRA, PROMT, RTECS*, TOXLINE, TOXLIT, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
4171 REFERENCES IN FILE CA (1967 TO DATE)
21 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
4178 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:325680

REFERENCE 2: 133:325454

REFERENCE 3: 133:323314

REFERENCE 4: 133:313639

REFERENCE 5: 133:313636

REFERENCE 6: 133:313600

REFERENCE 7: 133:310438

REFERENCE 8: 133:305085

REFERENCE 9: 133:301618

REFERENCE 10: 133:301262

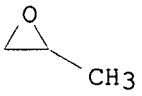
L14 ANSWER 8 OF 8 REGISTRY COPYRIGHT 2000 ACS

RN **9003-11-6** REGISTRY
CN Oxirane, methyl-, polymer with oxirane (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 50MB-26X
CN 75H380000
CN 75H90000
CN Actinol P 3035
CN Adeka Carpol MH 150
CN Adeka Carpol MH 500
CN Adeka Carpol PH 2000
CN Adeka CM 294
CN Adeka PR 3007
CN Adekanol NP 1200
CN Balab 615
CN Berol 370
CN Berol TVM 370
CN Bloatguard
CN Breox 50A1000
CN Breox 75W270
CN BSP 5000
CN Carpol 2040
CN Carpol 2050
CN CE
CN CF 0802
CN Desmophen 7100
CN Dezemulsionat E 96
CN Dissolvan 4411
CN Emkalyx EP 64
CN Emkalyx L 101
CN Emulgen PP
CN Emulgen PP 150
CN Emulgen PP 250
CN Emulgen PP 290
CN Epan 420
CN Epan 450
CN Epan 610
CN Epan 710
CN Epan 720
CN Epan 740
CN Epan 742
CN Epan 750
CN Epan U 102
CN Epan U 103
CN Epan U 105
CN Epan U 180
CN Ethylene glycol polyethylene-polypropylene glycol ether (1:2)
CN Ethylene glycol-propylene glycol copolymer
CN Ethylene glycol-propylene glycol polymer
CN Ethylene oxide-propylene oxide copolymer
CN Ethylene oxide-propylene oxide copolymer ethylene glycol ether
CN Excenol 2026T
CN Exocorpol
CN FT 257
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for DISPLAY
AR 53637-25-5
DR 12676-40-3, 12772-49-5, 9003-12-7, 9009-02-3, 9009-03-4, 9009-04-5, 9009-05-6, 9009-06-7, 9010-49-5, 9010-97-3, 9015-66-1, 9050-44-6, 9061-69-2, 9067-43-0, 167267-50-7, 168018-54-0, 163032-64-2, 163063-49-8, 162627-00-1, 53637-72-2, 57971-91-2, 58968-65-3, 56730-46-2, 57219-38-2, 57571-70-7, 124057-63-2, 59494-33-6, 59794-22-8, 60328-61-2, 64940-96-1, 66746-25-6, 106717-66-2, 50643-24-8, 51312-31-3, 51569-27-8, 60976-75-2, 37211-19-1, 37211-20-4, 37211-21-5, 37211-22-6, 37211-23-7, 37211-24-8, 37221-18-4, 37265-39-7, 37307-38-3, 37331-16-1, 37331-17-2, 37341-81-4, 70213-25-1, 72319-37-0, 73158-62-0, 70644-95-0, 71343-56-1, 77448-18-1, 77752-09-1, 76050-76-5, 86249-84-5, 86304-35-0, 81180-56-5, 87912-55-8,

39277-80-0, 39316-56-8, 39316-57-9, 39364-13-1, 39387-54-7, 208342-25-0, 232598-91-3, 250780-00-8, 291775-89-8
MF (C3 H6 O . C2 H4 O)x
CI PMS, COM
PCT Polyether, Polyether formed
LC STN Files: AGRICOLA, AIDSLINE, ANABSTR, APILIT, APILIT2, APIPAT, APIPAT2, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CBNB, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PHAR, PIRA, PROMT, RTECS*, TOXLINE, TOXLIT, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, TSCA**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

CM 1

CRN 75-56-9
CMF C3 H6 O



CM 2

CRN 75-21-8
CMF C2 H4 O

7228 REFERENCES IN FILE CA (1967 TO DATE)
2256 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
7237 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:325554

REFERENCE 2: 133:311185

REFERENCE 3: 133:310285

REFERENCE 4: 133:301003

REFERENCE 5: 133:298641

REFERENCE 6: 133:298048

REFERENCE 7: 133:298045

REFERENCE 8: 133:297705

REFERENCE 9: 133:297624

REFERENCE 10: 133:297600

10/037,064

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SHOW FILES
File   5:Biosis Previews(R) 1969-2000/Nov W4
         (c) 2000 BIOSIS
File  15:ABI/Inform(R) 1971-2000/Nov 23
         (c) 2000 Bell & Howell
File  34:SciSearch(R) Cited Ref Sci 1990-2000/Nov W3
         (c) 2000 Inst for Sci Info
File 144:Pascal 1973-2000/Nov W3
         (c) 2000 INIST/CNRS
File 155:MEDLINE(R) 1966-2000/Dec W4
         (c) format only 2000 Dialog Corporation
File 351:Derwent WPI 1963-2000/UD,UM &UP=200059
         (c) 2000 Derwent Info Ltd
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?
?DS

Set     Items   Description
S1     192828   (PEG? OR (POLY(W)ETHYLENE OR POLYETHYLENE OR ETHYLENE)(5N)-
             GLYCOL? OR POLYETHYLENEGLYCOL? OR ETHYLENEGLYCOL? OR ALKASURF?
              OR ANTAROX? OR CEMULSOL? OR CHARGE(W)E OR DELONIC? OR DISPON-
             IL? OR EMULGEN? OR ETHYLAN? OR HS(W)(2045 OR 208 OR 215))
S2     847787   S1 OR HYDROL? OR HYONIC? OR IGEPAL? OR INVADIN? OR MACOL? -
             OR MARLOPHEN?
S3     105736   (INF? OR INTERFERON?)(5N)(ALPHA? OR ALFA?) OR ROFERON?
S4       7262   RIBAVIRIN OR ICN(W)1229 OR NSC(W)163039 OR RIBAMI? OR TRIB-
             AVIRIN? OR VILONA? OR VIRAMID? OR VIRAZOL?
S5         58   S2 AND S3 AND S4
S6         46   RD (unique items)
?
?T S6/3 AB/1-46

 6/AB/1     (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
(c) 2000 BIOSIS. All rts. reserv.

12757225   BIOSIS NO.: 200000510848
Prognostic factors and early predictability of sustained viral response
  (SVR) in patients treated with *pegylated* (40kDa) *interferon* *alfa*-2a
  (*PegasysTM*): A new profile.
AUTHOR: Lee Samuel S(a); Heathcote E J; Reddy K Rajender; Zeuzem Stefan;
  Fried Michael W; Wright Teresa L; Pockros Paul J; Haeussinger D; Smith
  Coleman; Pawlotsky Jean-Michel; Lin Amy; Pappas Stephen C
AUTHOR ADDRESS: (a)Univ of Calgary, Calgary, AB**Canada
JOURNAL: Hepatology  32 (4 Pt. 2):p370A October, 2000
MEDIUM: print
CONFERENCE/MEETING: 51st Annual Meeting and Postgraduate Courses of the
American Association for the Study of Liver Diseases  Dallas, Texas, USA
October 27-31, 2000
SPONSOR: American Association for the Study of Liver Diseases
ISSN: 0270-9139
RECORD TYPE: Citation
LANGUAGE: English
SUMMARY LANGUAGE: English


 6/AB/2     (Item 2 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
(c) 2000 BIOSIS. All rts. reserv.
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12757197 BIOSIS NO.: 200000510820
Improved work productivity, safety, and quality of life with *pegylated* (40kDa) *interferon* *alfa*-2a (*PEGASYSTM*) therapy in the treatment of chronic hepatitis C.
AUTHOR: Perrillo Robert P(a); Thuluvath Paul J; Rothstein Ken; Alam Imatiaz ; Palmer Melissa; Gordon Stuart; Pappas Stephen C
AUTHOR ADDRESS: (a)Ochsner Clin, New Orleans, LA**USA
JOURNAL: Hepatology 32 (4 Pt. 2):p362A October, 2000
MEDIUM: print
CONFERENCE/MEETING: 51st Annual Meeting and Postgraduate Courses of the American Association for the Study of Liver Diseases Dallas, Texas, USA October 27-31, 2000
SPONSOR: American Association for the Study of Liver Diseases
ISSN: 0270-9139
RECORD TYPE: Citation
LANGUAGE: English
SUMMARY LANGUAGE: English

6/AB/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12757190 BIOSIS NO.: 200000510813
High and low doses of *PEG*-*interferon* *alfa* 2b plus *Ribavirin* in "naive" patients with chronic hepatitis C genotype 1: Effects on early viral kinetics.
AUTHOR: Sanchez-Avila Juan F(a); Buti Maria(a); Martel Maria(a); Stalgis Carlos; Lafleur F; Cotrina Montserrat; Morral Sergio; Esteban Rafael; Guardia Jaume
AUTHOR ADDRESS: (a)Hosp Vall d'Hebron, Barcelona**Spain
JOURNAL: Hepatology 32 (4 Pt. 2):p359A October, 2000
MEDIUM: print
CONFERENCE/MEETING: 51st Annual Meeting and Postgraduate Courses of the American Association for the Study of Liver Diseases Dallas, Texas, USA October 27-31, 2000
SPONSOR: American Association for the Study of Liver Diseases
ISSN: 0270-9139
RECORD TYPE: Citation
LANGUAGE: English
SUMMARY LANGUAGE: English

6/AB/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12757172 BIOSIS NO.: 200000510795
Pegylated (40kDa) *interferon* *alfa*-2a (*PegasysTM*) is superior to *interferon* *alfa*-2a (*Roferon*-A(R)) in improving posttreatment histologic outcome in chronic hepatitis C patients 1584.
AUTHOR: Heathcote E J(a); Balart Luis A; Shiffman Mitchell L; Pockros Paul J; Lee Samuel S; Reddy K Rajender; Minuk Y Gerald; Bain Vince; Sherman Morris; Wright Teresa L; Reindollar Robert W; Brunda Michael J
AUTHOR ADDRESS: (a)Univ of Toronto, Toronto, ON**Canada
JOURNAL: Hepatology 32 (4 Pt. 2):p223A October, 2000
MEDIUM: print
CONFERENCE/MEETING: 51st Annual Meeting and Postgraduate Courses of the American Association for the Study of Liver Diseases Dallas, Texas, USA October 27-31, 2000

SPONSOR: American Association for the Study of Liver Diseases
ISSN: 0270-9139
RECORD TYPE: Citation
LANGUAGE: English
SUMMARY LANGUAGE: English

6/AB/5 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12753941 BIOSIS NO.: 200000507564
Peginterferon *alfa*-2b plus *ribavirin* compared to *interferon* *alfa* -2b plus *ribavirin* for the treatment of chronic hepatitis C: 24 Week treatment analysis of a multicenter, multinational phase III randomized controlled trial.
AUTHOR: Manns M P(a); McHutchison J G; Gordon S; Rustgi V; Shiffman M L; Lee W M; Ling M L; Cort Susannah; Albrecht Janice K
AUTHOR ADDRESS: (a)Medical Sch of Hannover, Hannover**Germany
JOURNAL: Hepatology 32 (4 Pt. 2):p297A October, 2000
MEDIUM: print
CONFERENCE/MEETING: 51st Annual Meeting and Postgraduate Courses of the American Association for the Study of Liver Diseases Dallas, Texas, USA October 27-31, 2000
SPONSOR: American Association for the Study of Liver Diseases
ISSN: 0270-9139
RECORD TYPE: Citation
LANGUAGE: English
SUMMARY LANGUAGE: English

6/AB/6 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12741814 BIOSIS NO.: 200000495437
Estimating the cost-effectiveness of *ribavirin* and *pegylated* *interferon* *alfa*-2b for chronic hepatitis C.
AUTHOR: Wong John B(a)
AUTHOR ADDRESS: (a)Tufts-New England Medical Ctr, Boston, MA**USA
JOURNAL: Hepatology 32 (4 Pt. 2):p425A October, 2000
MEDIUM: print
CONFERENCE/MEETING: 51st Annual Meeting and Postgraduate Courses of the American Association for the Study of Liver Diseases Dallas, Texas, USA October 27-31, 2000
SPONSOR: American Association for the Study of Liver Diseases
ISSN: 0270-9139
RECORD TYPE: Citation
LANGUAGE: English
SUMMARY LANGUAGE: English

6/AB/7 (Item 7 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12672882 BIOSIS NO.: 200000426384
A dose-ranging study of *pegylated* *interferon* *alfa*-2b and *ribavirin* in chronic hepatitis C.
AUTHOR: Glue Paul(a); Rouzier-Panis Regine; Raffanel Claude; Sabo Ron;

Gupta Samir K; Salfi Margaret; Jacobs Shiela; Clement Robert P; Hepatitis C Intervention Therapy Group.
AUTHOR ADDRESS: (a)Schering-Plough Research Institute, K-15-4455, 2015 Galloping Hill Rd, Kenilworth, NJ, 07033**USA
JOURNAL: Hepatology 32 (3):p647-653 September, 2000
MEDIUM: print
ISSN: 0270-9139
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: The objectives of this study were to assess the safety, pharmacokinetics, and efficacy of *pegylated* *interferon* *alfa*-2b (*PEG*-Intron) plus *ribavirin* in patients with chronic hepatitis C. A total of 72 patients (35 men/37 women, age range 20-68 years) with clinically compensated chronic hepatitis C virus (HCV) were enrolled into this open-label, randomized, active controlled study. Patients received either *PEG*-Intron 0.35, 0.7, or 1.4 mug/kg subcutaneously weekly for 24 weeks alone, or in combination with *ribavirin* 600, 800, or 1,000 to 1,200 mg orally daily. Patients were evaluated during treatment and after a 24-week follow-up period for safety and efficacy. Detailed pharmacokinetic assessments were performed at weeks 1 and 4. *PEG*-Intron alone produced expected dose-related reductions in white cells, neutrophils and platelets. Addition of *ribavirin* reduced hemoglobin levels in a dose-related manner, did not further reduce *PEG* -Intron-induced decreases in neutrophil or white cell count, and increased platelet counts. Neutrophil function tests (C5a and FMLP migration, killing curves) were unaltered. Reported adverse events (flu-like symptoms, asthenia) were qualitatively similar in all dose groups. Anti-HCV activity, as measured by loss of detectable serum HCV RNA (i.e. <100 copies/mL) at the end of treatment (week 24) and after 24 weeks of follow-up (week 48) showed dose-response trends for *PEG* -Intron. At each *PEG*-Intron dose level, anti-HCV activity was higher in patients coadministered *ribavirin* than in patients treated with *PEG* -Intron monotherapy. There was no evidence of pharmacokinetic interactions with either drug. We conclude that the safety and tolerability of combined *PEG*-Intron/*ribavirin* and *PEG*-Intron alone were comparable. Combined *PEG*-Intron/*ribavirin* showed dose-related synergistic anti-HCV effects, which were numerically superior to those obtained with *PEG*-Intron monotherapy.

6/AB/8 (Item 8 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12563614 BIOSIS NO.: 200000317116
Pegylated *interferon* *alfa*-2b (*PEG*-Intron) monotherapy is superior to *interferon* *alfa*-2b (Intron A) for the treatment of chronic hepatitis C.
AUTHOR: Trepo C; Lindsay K; Niederau C; Shiffman M; Gordon S; Hoefs J; Schiff E; Marcellin P; Bacon B; Fang J; Garaud J; Albrecht J
AUTHOR ADDRESS: (a)Hopital Hotel Dieu, Lyon**France
JOURNAL: Journal of Hepatology 32 (Supplement 2):p29 2000
MEDIUM: print
CONFERENCE/MEETING: 35th Annual Meeting of the European Association for the Study of the Liver Rotterdam, Netherlands April 29-May 03, 2000
SPONSOR: European Association for the Study of the Liver
ISSN: 0168-8278

RECORD TYPE: Citation
LANGUAGE: English
SUMMARY LANGUAGE: English

6/AB/9 (Item 9 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12537980 BIOSIS NO.: 200000291482
Pegylated *interferon* *alfa*-2a (*PEGASYSTM*) and *ribavirin* combination therapy for chronic hepatitis C: A phase II open-label study.
AUTHOR: Sulkowski Mark S; Reindollar Robert; Yu J
AUTHOR ADDRESS: (a)Johns Hopkins Univ Sch of Medicine, Baltimore, MD**USA
JOURNAL: Gastroenterology 118 (4 Suppl. 2 Part 1):pAASLD A950 April, 2000
MEDIUM: print.
CONFERENCE/MEETING: 101st Annual Meeting of the American Gastroenterological Association and the Digestive Disease Week. San Diego, California, USA May 21-24, 2000
SPONSOR: American Gastroenterological Association
ISSN: 0016-5085
RECORD TYPE: Citation
LANGUAGE: English
SUMMARY LANGUAGE: English

6/AB/10 (Item 10 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12428575 BIOSIS NO.: 200000182077
Pathogenesis, diagnosis and management of hepatitis C.
AUTHOR: Boyer Nathalie; Marcellin Patrick(a)
AUTHOR ADDRESS: (a)Service d'Hepatologie, Hopital Beaujon, 100 Bd. du General Leclerc, 92110, Clichy**France
JOURNAL: Journal of Hepatology 32 (Suppl. 1):p98-112 2000
ISSN: 0168-8278
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: The hepatitis C virus (HCV) is the leading cause of chronic liver disease worldwide. It is estimated that about 170 million people are chronically infected with HCV. Chronic hepatitis C is a major cause of cirrhosis and hepatocellular carcinoma and HCV-related endstage liver disease is, in many countries, the first cause of liver transplantation. HCV infection is characterized by its propensity to chronicity. Because of its high genetic variability, HCV has the capability to escape the immune response of the host. HCV is not directly cytopathic and liver lesions are mainly related to immune-mediated mechanisms, which are characterized by a predominant type 1 helper cell response. Co-factors influencing the outcome of the disease including age, gender and alcohol consumption are poorly understood and other factors such as immunologic and genetic factors may play an important role. Recent studies have shown that the combination therapy with *alpha* *interferon* and *ribavirin* induces a sustained virological response in about 40% of patients with chronic hepatitis C. The sustained response rates are mainly dependent on the viral genotype (roughly 60% in genotype non-1 and 30% in genotype 1). Reliable diagnostic tools are now available and useful for detecting HCV

infection, to quantify viral load and to determine the viral type. The assessment of the viral quasispecies and the characterization of viral sequences might be clinically relevant but standardized and simple techniques are needed. The lack of animal models and of in vitro culture systems hampers the understanding of the pathogenesis of chronic hepatitis C and the development of new antivirals. New therapeutic schedules with higher and/or daily doses of *alpha* *interferon* do not seem to improve the efficacy greatly. The conjugation with *polyethylene* *glycol* (*PEG*) improved the pharmacodynamics and the efficacy of *alpha* *interferon*. Emerging new therapies include inhibitors of viral enzymes (protease, helicase and polymerase), cytokines (IL-12 and IL-10), antisense oligonucleotides and ribozymes. The first candidate compounds should be available in the next few years. The development of an effective vaccine remains the most difficult and pressing challenge. Because of the high protein variability of HCV, protective vaccines could be extremely difficult to produce and therapeutic vaccines seem more realistic. Considerable progress has been made in the field of HCV since its discovery 10 years ago but a major effort needs to be made in the next decade to control HCV-related liver disease.

6/AB/11 (Item 11 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12356507 BIOSIS NO.: 200000110009
Treatment of chronic hepatitis C: Comparative virologic response rates among the different interferons.
AUTHOR: Lindsay Karen L(a)
AUTHOR ADDRESS: (a)Division of Gastroenterology and Liver Disease, University of Southern California, 1355 San Pablo Street, 1st Floor, Los Angeles, CA, 90033**USA
JOURNAL: Journal of Hepatology 31 (Suppl. 1):p232-236 1999
ISSN: 0168-8278
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: End-treatment and sustained virologic response rates are similar in large, comparative controlled trials which have compared the standard dosing regimens of *interferon* *alpha*-2b to *interferon* *alpha*-n1 and consensus *interferon*, as well as to virologic response rates recently reported with *interferon* *alpha*-2b monotherapy for 24 weeks. For patients who have responded and relapsed after an initial course of *alpha* *interferon*, retreatment with consensus *interferon* for 48 weeks demonstrates a high sustained virologic response rate, similar to that reported with *interferon* *alpha*-2b combined with *ribavirin* for 24 weeks. Based on available pharmacokinetic and pharmacodynamic data, *pegylation* of *interferon* *alpha*-2a shows promise in demonstrating high sustained serum levels and 2',5' OAS activity. Preliminary data from a Phase II clinical trial of a 48-week treatment in naive patients demonstrates end-treatment and sustained virologic response rates similar to that seen with *interferon* *alpha*-2b combined with *ribavirin* for 48 weeks.

6/AB/12 (Item 12 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12204922 BIOSIS NO.: 199900499771
Combination therapy with *peginterferon* alpha-2a (*PEG*-IFN) and *ribavirin* in the treatment of patients with chronic hepatitis C (CHC): A phase II open-label study.
AUTHOR: Sulkowski M(a); Reindollar R; Yu J
AUTHOR ADDRESS: (a)The Johns Hopkins Univ School of Medicine, Baltimore, MD **USA
JOURNAL: Hepatology 30 (4 PART 2):p197A Oct., 1999
CONFERENCE/MEETING: 50th Annual Meeting and Postgraduate Courses of the American Association for the Study of Liver Diseases Dallas, Texas, USA November 5-9, 1999
SPONSOR: American Association for the Study of Liver Diseases
ISSN: 0270-9139
RECORD TYPE: Citation
LANGUAGE: English

6/AB/13 (Item 13 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12191726 BIOSIS NO.: 199900486575
A dose-ranging study of *PEG*-Intron and *ribavirin* in chronic hepatitis C: Safety, efficacy, and virologic rationale.
AUTHOR: Glue Paul(a); Rouzier-Panis R; Raffanel C; Sabo R; Gupta S K; Jacobs S; Clement R P; Ingravallo P; Zhong W; Hong Z; Garaud J J; Lau Jyn
AUTHOR ADDRESS: (a)Schering-Plough Res Institute, Kenilworth, NJ**USA
JOURNAL: Hepatology 30 (4 PART 2):p303A Oct., 1999
CONFERENCE/MEETING: 50th Annual Meeting and Postgraduate Courses of the American Association for the Study of Liver Diseases Dallas, Texas, USA November 5-9, 1999
SPONSOR: American Association for the Study of Liver Diseases
ISSN: 0270-9139
RECORD TYPE: Citation
LANGUAGE: English

6/AB/14 (Item 14 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11386392 BIOSIS NO.: 199800167724
Oral enzyme therapy in hepatitis C patients.
AUTHOR: Stauder G(a); Kabil S
AUTHOR ADDRESS: (a)Mucos Pharma, Clin. Res., Malvenweg 2, D-82538 Geretsried**Germany
JOURNAL: International Journal of Immunotherapy 13 (3-4):p153-158 1997
ISSN: 0255-9625
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: In an open, randomized, clinical pilot trial, four groups with 20 hepatitis C patients each were treated with either 'liver support' therapy, with established medications (one group with *ribavirin*, one group with *alpha*-*interferon*), or with a novel oral test drug, Phlogenzym a combination of *hydrolytic* enzymes with the flavonoid rutosid. The liver transaminases, AST, ALT and S-gamma-GT markedly improved over the period of three months in the three drug groups, but

only marginally in the liver support group, The best results were found with Phlogenzym which was even superior to *ribavirin* and *alpha*-*interferon*. The tolerance of the oral enzymes was excellent. Further clinical trials with longer observation times, greater numbers of patients, double-blind and partly placebo-controlled, are under way.

6/AB/15 (Item 1 from file: 15)
DIALOG(R)File 15:ABI/Inform(R)

02082518 63383152
Filling the biopharmaceutical pipeline
Boswell, Clay
Chemical Market Reporter v258n18 PP: FR33-FR37 Oct 30, 2000 ISSN: 1092-0110 JRNL CODE: CHM
WORD COUNT: 2402

ABSTRACT: After the optimism of the 1980s and the caution of the 1990s, biopharmaceuticals are finally beginning to realize their potential. Four biopharmaceutical products had sales over $1 billion last year, total sales for the nearly 100 marketed globally exceeded $20 billion, and the industry pipeline is beginning to swell. Biopharmaceuticals can be divided into five categories on the basis of their form: proteins, antibodies, nucleic acids, glycotherapeutics, and cell- or tissue-based therapeutics. On the market, the most successful of these have been proteins, which accounted for 27 of the top 30 biopharmaceuticals in 1999. Protein drugs can in turn be classified by function as cytokines, hormones, clotting factors, tissue plasminogen activators and antigens (vaccines).

6/AB/16 (Item 2 from file: 15)
DIALOG(R)File 15:ABI/Inform(R)

02082517 63382865
Active pharmaceutical ingredients: The opportunities in the branded prescription market
Van Arnum, Patricia
Chemical Market Reporter v258n18 PP: FR14-FR32 Oct 30, 2000 ISSN: 1092-0110 JRNL CODE: CHM
WORD COUNT: 6643

ABSTRACT: The supply of active pharmaceutical ingredients to the branded prescription market is a key outlet for fine chemical producers. Much of the optimism for the custom manufacturing market relies on the expectations for increased drug output by the major pharmaceutical companies. Despite all the attention given to new product development, drug productivity remains fairly consistent with historical levels. A company-by-company analysis of the top drug companies reveals a reliance on established products, product line extensions through new indications and, for certain companies, significant generic defense efforts as key drugs come off patent.

6/AB/17 (Item 3 from file: 15)
DIALOG(R)File 15:ABI/Inform(R)

02082513 63382854
Pharma majors post strong results
Anonymous
Chemical Market Reporter v258n18 PP: 24 Oct 30, 2000 ISSN: 1092-0110
JRNL CODE: CHM
WORD COUNT: 303

ABSTRACT: Third quarter earnings from major pharmaceutical companies were generally strong. Pfizer Inc. and Schering-Plough Corporation each posted results in the high-single digits, and Merck & Co. Inc., with gains from both its pharmaceutical and managed care businesses, reported a 29% gain in sales.

6/AB/18 (Item 4 from file: 15)
DIALOG(R)File 15:ABI/Inform(R)

00740463 93-89684
1993 health-care agency profiles
Anonymous
Medical Marketing & Media v28n7 PP: 20-76 Jul 1993 ISSN: 0025-7354
JRNL CODE: MMM
WORD COUNT: 14124

ABSTRACT: Some advertising agencies responding to Medical Marketing & Media's 1993 survey, predict that 1993 will be a banner year despite the political and economic uncertainties that face many of their clients as they anticipate the results of health care reform and the possible impact on pricing. Of the 107 agencies responding to the survey, 56 say that business is up so far in 1993, compared to 1992. Another 16 report incomes are steady at 1992 levels. Increases in gross income range from over 100% for 2 agencies to single digits for about a dozen respondents. Twelve agencies list overseas affiliates. Agencies that provided figures for their 1992 billings or for their billing breakdown by media-source are profiled.

6/AB/19 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

09003549 Genuine Article#: 355FX Number of References: 36
Title: Hepatitis C: Current and future treatment
Author(s): Keeffe EB (REPRINT)
Corporate Source: STANFORD UNIV,MED CTR, LIVER TRANSPLANT PROGRAM/STANFORD//CA/94305 (REPRINT)
Journal: INFECTIONS IN MEDICINE, 2000, V17, N9 (SEP), P603-&
ISSN: 0749-6524 Publication date: 20000900
Publisher: SCP COMMUNICATIONS INC, 134 W 29TH ST, NEW YORK, NY 10001-5304
Language: English Document Type: ARTICLE
Abstract: *Interferon* *alfa*-2b, 3 million units tiw, plus *ribavirin*, 1000 to 1200 mg daily for 6 to 12 months, has shown an improvement of 2-fold or more for all measures of efficacy when compared with interferon monotherapy. Ln the next year, treatment of chronic hepatitis C will involve *pegylated* interferons, either alone or in combination with *ribavirin*. Therapy in 3 to 5 years will likely be multidrug combinations, including inhibitors of the hepatitis C virus

(HCV) protease, helicase, or polymerase, with the aim of reducing serum levels or eradicating HCV RNA.

6/AB/20 (Item 2 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

08966368 Genuine Article#: 350LA Number of References: 62
Title: Treatment of chronic hepatitis C virus infection in patients with cirrhosis
Author(s): Zeuzem S (REPRINT)
Corporate Source: UNIV FRANKFURT KLINIKUM,ZENTRUM INNEREN MED, MED KLIN 2, THEODOR STERN KAI 7/D-60590 FRANKFURT//GERMANY/ (REPRINT)
Journal: JOURNAL OF VIRAL HEPATITIS, 2000, V7, N5 (SEP), P327-334
ISSN: 1352-0504 Publication date: 20000900
Publisher: BLACKWELL SCIENCE LTD, P O BOX 88, OSNEY MEAD, OXFORD OX2 0NE, OXON, ENGLAND
Language: English Document Type: REVIEW
Abstract: Chronic hepatitis C virus (HCV) infection eventually leads to cirrhosis in 20-30% of patients and to hepatocellular carcinoma (HCC) in 1-5% of patients. Rates of sustained virological response with standard *interferon*-*alpha* (IFN-*alpha*) are low in patients without cirrhosis (generally < 20%) and are even lower in those with cirrhosis. Combination therapy with IFN and *ribavirin* improves response rates in patients with chronic hepatitis C without cirrhosis, and the results from subgroups of HCV-infected patients with advanced fibrosis or cirrhosis are encouraging. Importantly, treatment with IFN slows progression of liver fibrosis, regardless of HCV genotype or early response to therapy, and reduces the risk of HCC by two- to fivefold. The risk of development of HCC is also lower in patients who show at least a partial response to IFN therapy compared with those who show no response. There is a clear need for more definitive studies of treatment in patients with chronic hepatitis C and cirrhosis, ideally using therapies with greater efficacy. Nonetheless, based on the potential to slow the progression of liver fibrosis (regardless of treatment response) and to reduce the risk of HCC, a greater number of HCV-infected patients with cirrhosis should be considered as candidates for IFN treatment. Preliminary data indicate that *pegylated* IFNs have improved virological response rates and may have additional clinical benefits in the prevention or reduction of fibrosis and retardation of progression of cirrhosis and HCC in these patients.

6/AB/21 (Item 3 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

08861837 Genuine Article#: 337LE Number of References: 26
Title: Firstline treatment for hepatitis C: combination interferon/*ribavirin* versus interferon monotherapy
Author(s): Lai MY (REPRINT)
Corporate Source: NATL TAIWAN UNIV,COLL MED, GRAD INST CLIN MED/TAIPEI 10018//TAIWAN/ (REPRINT)
Journal: JOURNAL OF GASTROENTEROLOGY AND HEPATOLOGY, 2000, V15, S (MAY), P E130-E133
ISSN: 0815-9319 Publication date: 20000500
Publisher: BLACKWELL SCIENCE ASIA, 54 UNIVERSITY ST, P O BOX 378, CARLTON VICTORIA 3053, AUSTRALIA
Language: English Document Type: ARTICLE

Abstract: In the initial treatment of chronic hepatitis C, *interferon*-*alfa* (IFN-*alpha*) monotherapy for 24-48 weeks induces sustained response rates of only 10-20%. Combination therapy with IFN-alpha plus *ribavirin* induces a sustained response in 40-50% of patients, and can be now recommended as the firstline therapy for chronic hepatitis C. Stopping therapy at week 12 because of persistent viraemia is unnecessary with the combination therapy because later clearance of HCV RNA can still occur with a sustained response. Patients with HCV genotype 1 should receive 48 weeks of combination therapy, in contrast to 24 weeks for patients with genotypes 2 or 3. For patients who cannot tolerate the side effects of *ribavirin*, such as anaemia, IFN-alpha at 3 MU three times weekly for 48 weeks is preferred as the initial therapy. The long-acting *pegylated* IFN can be expected to enhance the efficacy of combination therapy in the treatment of chronic hepatitis C and appears to be much more potent as monotherapy. Further studies are needed to improve the current 'half-full' status of chronic hepatitis C treatment. (C) 2000 Blackwell Science Asia Pty Ltd.

6/AB/22 (Item 4 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

08816375 Genuine Article#: 309RU Number of References: 0
Title: *Pegylated* *interferon* *alfa*-2a (*pegasys*(TM)) and *ribavirin* combination therapy for chronic hepatitis C: A phase II open-label study.
Author(s): Sulkowski MS; Reindollar R; Yu J
Corporate Source: JOHNS HOPKINS UNIV,SCH MED/BALTIMORE//MD/; CAROLINAS CTR LIVER DIS,/CHARLOTTE//NC/; HOFFMANN LA ROCHE,/NUTLEY//NJ/
Journal: GASTROENTEROLOGY, 2000, V118, N4,1,2 (APR), P236-236
ISSN: 0016-5085 Publication date: 20000400
Publisher: W B SAUNDERS CO, INDEPENDENCE SQUARE WEST CURTIS CENTER, STE 300, PHILADELPHIA, PA 19106-3399
Language: English Document Type: MEETING ABSTRACT

6/AB/23 (Item 5 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

08775377 Genuine Article#: 327VW Number of References: 30
Title: Therapeutic options for HCV - management of the infected individual
Author(s): Foster GR (REPRINT)
Corporate Source: ST MARYS HOSP,IMPERIAL COLL SCH MED, DEPT MED, CTR LIVER, QEQM WING, PRAED ST/LONDON W2 1PG//ENGLAND/ (REPRINT)
Journal: BEST PRACTICE & RESEARCH IN CLINICAL GASTROENTEROLOGY, 2000, V14, N2 (APR), P255-264
ISSN: 1521-6918 Publication date: 20000400
Publisher: BAILLIERE TINDALL, 24-28 OVAL RD, LONDON NW1 7DX, ENGLAND
Language: English Document Type: ARTICLE
Abstract: Patients with chronic hepatitis C infection should be assessed by liver biopsy prior to consideration of anti-viral therapy. Patients with histologically mild disease should be observed at regular intervals and assessed with a repeat liver biopsy after an interval of 3-4 years. Those with severe disease should receive early treatment with interferon-se and *ribavirin*. The duration of therapy is determined by the genotype of the infecting virus-viral genotypes 2 and 3 require only 6 months of treatment but other genotypes should be treated for 12 months. Approximately 35-40% of treated patients will

respond to therapy with a permanent cessation of viral replication and improvement in liver histology. New therapies including *polyethylene* *glycol*, *PEGylated*, interferons and combination regimes involving amantadine are currently under evaluation and it is hoped that improved regimes will be developed in the near future.

6/AB/24 (Item 6 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

08761195 Genuine Article#: 327KB Number of References: 7
Title: Coinfection by HIV and hepatitis C virus
Author(s): Perronne C (REPRINT) ; BaniSadr F
Corporate Source: HOP UNIV RAYMOND POINCARE,FAC MED PARIS OUEST, SERV MALAD INFECT & TROP/F-92380 GARCHES//FRANCE/ (REPRINT)
Journal: MEDECINE ET MALADIES INFECTIEUSES, 2000, V30, N6 (JUN), P344-346
ISSN: 0399-077X Publication date: 20000600
Publisher: EDITIONS SCIENTIFIQUES MEDICALES ELSEVIER, 23 RUE LINOIS, 75724 PARIS CEDEX 15, FRANCE
Language: French Document Type: EDITORIAL MATERIAL

6/AB/25 (Item 7 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

08683515 Genuine Article#: 317AC Number of References: 89
Title: Antiviral therapy of hepatitis C
Author(s): Erhardt A (REPRINT) ; Petry W; Ebel M; Jablonowski H; Heintges T ; Haussinger D
Corporate Source: UNIV DUSSELDORF,KLIN GASTROENTEROL HEPATOL & INFEKTIOL, MOORENSTR 5/D-40225 DUSSELDORF//GERMANY/ (REPRINT)
Journal: ZEITSCHRIFT FUR GASTROENTEROLOGIE, 2000, V38, N3 (MAR), P259-269
ISSN: 0044-2771 Publication date: 20000300
Publisher: DEMETER VERLAG GEORG THIEME VERLAG, PETRA SCHLAGENHAUF, RUDIGERSTR 14, D-70469 STUTTGART, GERMANY
Language: German Document Type: REVIEW
Abstract: Hepatitis C is one of the world's leading infectious diseases. The interferon-*ribavirin* combination therapy is the new standard for the treatment of hepatitis C in naive and relapse patients. Virological sustained response rates can be more than doubled by the IFN-*ribavirin* combination therapy compared to IFN-monotherapy and treatment duration can be reduced to six months in many cases. The IFN-*ribavirin* combination therapy has a high relative benefit in patients with unfavorable predictive parameters like high viral load, HCV genotype-1 infection and compensated Liver cirrhosis. Anemia is the most important side effect of the guanosin analogue *ribavirin*. There - are no official therapeutic recommendations for non-responder patients at present. These patients should be treated within controlled clinical trials. Monotherapy with *PEG*(*pegylated*)-interferons and combination therapies with *PEG*-interferons and *ribavirin* are the most promising future therapeutic options.

6/AB/26 (Item 8 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

08565258 Genuine Article#: 301NV Number of References: 39

Title: Coinfection with the hepatitis C virus and HIV: current aspects
Author(s): BaniSadr F (REPRINT) ; Perronne C
Corporate Source: HOP UNIV RAYMOND POINCARE,FAC MED PARIS OUEST, SERV MALAD INFECT & TROP, 104 BLVD RAYMOND POINCARE/F-92380 GARCHES//FRANCE/ (REPRINT)
Journal: MEDECINE ET MALADIES INFECTIEUSES, 2000, V30, 1 (MAR), PS43-S48
ISSN: 0399-077X Publication date: 20000300
Publisher: EDITIONS SCIENTIFIQUES MEDICALES ELSEVIER, 23 RUE LINOIS, 75724 PARIS CEDEX 15, FRANCE
Language: French Document Type: ARTICLE
Abstract: The treatment of coinfection with the hepatitis C virus (HCV) in HIV-infected patients was rarely discussed before the era of the HIV protease inhibitors, since the response to monotherapy with *interferon* *alpha* (*INF* *alpha*) was poor, with a mean prognosis of the HIV disease estimated at around ten years. In the present context, monitoring is reconsidered. The HIV-associated immunosuppression may be responsible fora false negativity of some serologic tests for HCV. The HIV-HCV coinfection increases the risk of maternofoetal transmission of HCV. Studies evaluating the influence of the HIV coinfection on the natural history of the HCV infection show its deleterious role. The immune restoration obtained with the highly active antiretroviral therapies is not linked with a decrease of the HCV viral load. The HIV-HCV coinfection is responsible for a threefold increase of the risk of elevation of seric transaminases when an antiretroviral treatment is given. The immune restoration obtained with an antiretroviral treatment may reveal the HCV infection and favor a rapid aggravation of hepatic histology and evolution toward cirrhosis. HCV-associated complications may become a major factor of morbidity and mortality, leading to the need for an anti-hepatitis C treatment in HIV-*infected* patients. The combination of *INF* *alpha* and *ribavirin* seems to be the best treatment, Its efficacy and tolerability must be evaluated in HIV-infected patients. Drug interactions are likely to occur, and *INF* *alpha*, like *ribavirin*, may favor CD4 lymphopenia. A new form of *INF* *alpha* with a prolonged half-life (*PEG*-*INF* *alpha*) seems to be promising. (C) 2000 Editions scientifiques et medicales Elsevier SAS.

6/AB/27 (Item 9 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

08376330 Genuine Article#: 278HU Number of References: 20
Title: Clinical implications of hepatitis C viral kinetics
Author(s): Zeuzem S (REPRINT)
Corporate Source: UNIV FRANKFURT KLINIKUM,ZENTRUM INNEREN MED, MED KLIN 2, THEODOR-STERN-KAI 7/D-60590 FRANKFURT//GERMANY/ (REPRINT)
Journal: JOURNAL OF HEPATOLOGY, 1999, V31, 1, P61-64
ISSN: 0168-8278 Publication date: 19990000
Publisher: MUNKSGAARD INT PUBL LTD, 35 NORRE SOGADE, PO BOX 2148, DK-1016 COPENHAGEN, DENMARK
Language: English Document Type: ARTICLE
Abstract: Antiviral treatment of patients with chronic hepatitis C can perturb the steady-state of virus production and clearance. From serial measurements of changes in viremia, kinetic information on the dynamics of hepatitis C virus (HCV) replication can be obtained. After a delay of about 9 h due to *interferon*-*alpha* pharmacokinetics, the decline of viremia in patients treated with *interferon*-*alpha* is characterized by a concave shape. In the first phase (day 1) a rapid dose-dependent decline in viral load is observed. The second phase

viral decline (greater than or equal to day 2) shows a much slower decline with no or less pronounced differences between the applied *interferon*-*alpha* schedules. While a first phase decline can be observed in almost all patients treated with *interferon*-*alpha*, non-responders typically reveal no further decline of viremia during the second phase. Kinetic analysis showed that combination therapy with *interferon*-*alpha* plus *ribavirin* has no direct synergistic antiviral effect in the initial 4 weeks of treatment of HCV-*infected* patients with 6 MU IFN *alpha* three times per week. Calculations revealed a minimum virus production and clearance per day in patients with chronic hepatitis C of approximately 10(10)-10(12) virions per day and an in vivo half-life of the virus in the order of a few hours. The high turnover rates of HCV explain the rapid generation of viral diversity and the opportunity for viral escape from the host immune surveillance and antiviral therapy. The implications derived from HCV kinetics comprise the consideration of more aggressive initial dosing regimens (especially daily doses), the possibility to optimize therapy individually not only according to pretreatment parameters but also according to the initial decline of viral load and the perception that eradication of the virus will rely on the half-life of infected cells.

6/AB/28 (Item 10 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

08232249 Genuine Article#: 260TU Number of References: 82
Title: Characteristics of hepatitis C-virus and viral predictors of therapeutical response
Author(s): Ambrosch A (REPRINT) ; Konig W
Corporate Source: UNIV KLIN,INST MIKROBIOL, LEIPZIGER STR 44/D-39120 MAGDEBURG//GERMANY/ (REPRINT); OTTO VON GUERICKE UNIV,INST MIKROBIOL/MAGDEBURG//GERMANY/
Journal: MEDIZINISCHE KLINIK, 1999, V94, N11 (NOV 15), P626-632
ISSN: 0723-5003 Publication date: 19991115
Publisher: URBAN & VOGEL, LINDWURMSTRASSE 95, D-80337 MUNICH, GERMANY
Language: German Document Type: REVIEW
Abstract: square Natural History of Hepatitis C-Infection and Viral Characteristics: Hepatitis C-virus (HCV) infection is a major cause of non-A, non-B-hepatitis and, additionally, is associated with liver cirrhosis and hepato-cellular carcinoma. The high degree of chronificity of HCV-infection is reasonable due to antigenic variability of neutralizing epitopes leading to incomplete immunoresponse with sublity of neutralizing epitopes leading to incomplete immunoresponce with subsequent virus persistence. Besides genetic variants of HCV within a virus population (quasispecies nature of HCV), different genotypes are classified being genetically and phenotypically distinct, and geographically restricted in part. Genotyping of HCV is not only important for phylogenetic and epidemiological studies, but also a prodictive marker for pathogenesis and therapy.

square Viral Predictors of HCV Therapy: In a meta-analysis of 18 therapeutical studies of chronical HCV infections, genotype 1 and high levels of viremia determined markedly the response to interferon therapy. In this context, clinical trials have proven the effect of a combined therapy with interferon and *ribavirin*. Especially patients with HCV genotype 1 or high levels of viremia had a real benefit from combined antiviral therapy in comparison to monotherapy with interferon.

square Conclusion and Future Concepts: Besides recent concepts improving the therapeutical response to HCV infection, further effort is necessary to develop more successful strategies for eradication of hepatitis C virus. In this context, variations of interferon therapy should be evaluated (e.g. higher and daily doses, longer duration of interferon therapy, ''retarded'' interferon (*PEG*-IFN). In addinon, new therapeutical concepts should be performed including a combination of interferon with other known antiviral agents (amantadine), a combination with immunomodulators (GM-CSF, thymosin alpha 1), the development of new antiviral agents (inhibitors of viral proteases, helicases and polymerases) and the exploration of anti-viral, molecular strategies (specific ribozymes, antisense oligonucleotides and DNA-vaccination). Nevertheless, the development of an effective vaccination should be the most important challenge for the future.

6/AB/29 (Item 11 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

08208843 Genuine Article#: 258KL Number of References: 58
Title: Treatment of hepatitis C
Author(s): Erhardt A (REPRINT) ; Petry W; Kappert G; Heintges T; Haussinger D
Corporate Source: UNIV DUSSELDORF,KLIN GASTROENTEROL HEPATOL & INFEKTIOL, MOORENSTR 5/D-40225 DUSSELDORF//GERMANY/ (REPRINT)
Journal: MEDIZINISCHE WELT, 1999, V50, N10 (OCT), P426-432
ISSN: 0025-8512 Publication date: 19991000
Publisher: F K SCHATTAUER VERLAG GMBH, P O BOX 10 45 43, LENZHALDE 3, D-70040 STUTTGART, GERMANY
Language: German Document Type: ARTICLE
Abstract: Hepatitis C is one of the world's leading infectious diseases; With an interferon monotherapy sustained virological response rates of only 10-20% can be achieved in naive patients with chronic hepatitis C. The new combination therapy of interferon and *ribavirin* can achieve more than doubled sustained virological response rates in naive patients. In patients, who relapsed after an IFN monotherapy, sustained response rates of 50% could be achieved by IFN-*ribavirin* therapy. Thus, combination of interferon and *ribavirin* has to be referred to as new standard in the therapy of hepatitis C. *Ribavirin* is a guanosine analogue, the most common side effect is hemolytic anemia. IFN-*ribavirin* therapy was ineffective for retherapy of IFN-nonresponder patients. Extension of combination therapies, induction therapies with daily IFN-dosing, the administration of *pegylated* interferons and new drugs like protease-/helicase-inhibitors, amantadine, thymosine are possible future therapeutic options.

6/AB/30 (Item 12 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

07986324 Genuine Article#: 232MG Number of References: 110
Title: Developments in hepatitis C during 1997-1999
Author(s): Poordad FF (REPRINT) ; Gish RG
Corporate Source: JOHNS HOPKINS UNIV,SCH MED, DEPT MED, DIV GASTROENTEROL, 1830 E MONUMENT ST, 423/BALTIMORE//MD/21205 (REPRINT)
Journal: EXPERT OPINION ON THERAPEUTIC PATENTS, 1999, V9, N9 (SEP), P

1249-1262
ISSN: 1354-3776 Publication date: 19990900
Publisher: ASHLEY PUBL LTD, 1ST FL, THE LIBRARY, 1 SHEPHERDS HILL HIGHGATE, LONDON N6 5QJ, ENGLAND
Language: English Document Type: REVIEW
Abstract: Hepatitis C has became an area of intensive research over the past several years. With current worldwide prevalence estimated at 150 to 200 million people, and with almost four million Americans infected, ii is a major public health issue [1]. Of those infected, over 85% will develop chronic infection [2,3]. of those who develop chronic infection, 20% will develop cirrhosis, and in the cirrhotic population, 20% develop hepatocellular carcinoma [4]. It is still difficult in the early stages of disease to determine who is at risk of developing cirrhosis, and therefore who would benefit most from therapy. manifestations of the disease that lead clinicians to initiate therapy [5]. The However, even in the non-cirrhotic individual, there are many symptomatic ultimate goal of treatment is to achieve sustained eradication of the virus. Until recently, the mainstay of treatment has been interferon (IFN-) monotherapy, which is less than 25% effective and is generally accompanied by side effects. Newer therapeutic modalities focus on less toxic compounds, targeting viral proteins such as protease or helicase, or viral genomic segments with antisense peptides and ribozymes. This chapter is an overiview of the patent literature from 1997 to mid-1999 and discusses possible new treatement options including vaccines and delivery systems to cells (Figure 1).

6/AB/31 (Item 13 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

07795351 Genuine Article#: 209DU Number of References: 49
Title: Treatment strategies for chronic hepatitis C: Update since the 1997 National Institutes of Health Consensus Development Conference
Author(s): Ahmed A; Keeffe EB (REPRINT)
Corporate Source: STANFORD UNIV,MED CTR, 750 WELCH RD, SUITE 210/PALO ALTO//CA/94304 (REPRINT); STANFORD UNIV,SCH MED, DIV GASTROENTEROL, DEPT MED/STANFORD//CA/94305
Journal: JOURNAL OF GASTROENTEROLOGY AND HEPATOLOGY, 1999, V14, S (MAY), P S12-S18
ISSN: 0815-9319 Publication date: 19990500
Publisher: BLACKWELL SCIENCE ASIA, 54 UNIVERSITY ST, P O BOX 378, CARLTON VICTORIA 3053, AUSTRALIA
Language: English Document Type: ARTICLE
Abstract: The National Institutes of Health Consensus Development Conference on the management of hepatitis C, which took place in March 1997 and was published in September 1997, established guidelines for the diagnosis and management of chronic hepatitis C. The recommended treatment of chronic hepatitis C virus (HCV) *infection* is *interferon* *alpha* (or equivalent) 3 MIU three times per week for 12 months, in patients showing response to therapy after 3 months. Patients with the greatest risk for progression to cirrhosis (i.e. persistently elevated alanine aminotransferase levels, detectable serum HCV-RNA and liver biopsy showing portal or bridging fibrosis and at least moderate inflammation and necrosis) are recommended as candidates for therapy. The indication for therapy is less obvious in patients with milder histological changes, compensated cirrhosis and age less than 18 years or older than 60 years. Treatment is not indicated for patients with persistently normal aminotransferases or decompensated cirrhosis. This review outlines the background studies that led to the

recommendations of the National Institutes of Health for the treatment of chronic hepatitis C and reviews newer evolving treatment strategies over the past year. In particular, the results of studies exploring treatment: options for relapsers and non-responders to prior interferon therapy and the reported results to date on the safety and efficacy of combination therapy with interferon plus *ribavirin* are highlighted. Although aggressive suppression of HCV-RNA with induction therapy (daily and/or higher doses) or long-acting *pegylated* interferon preparations may improve the current results of therapy, few data are yet available. Finally, the treatment of chronic hepatitis C with protease inhibitors holds promise but has yet to reach the stage of clinical trials.

6/AB/32 (Item 14 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

06204591 Genuine Article#: YB712 Number of References: 194
Title: In search of a selective antiviral chemotherapy
Author(s): DeClercq E (REPRINT)
Corporate Source: UNIV CATHOLIQUE LOUVAIN,REGA INST MED RES, MINDERBROEDERSSTR 10/B-3000 LOUVAIN//BELGIUM/ (REPRINT)
Journal: CLINICAL MICROBIOLOGY REVIEWS, 1997, V10, N4 (OCT), P674-&
ISSN: 0893-8512 Publication date: 19971000
Publisher: AMER SOC MICROBIOLOGY, 1325 MASSACHUSETTS AVENUE, NW, WASHINGTON, DC 20005-4171
Language: English Document Type: REVIEW

6/AB/33 (Item 1 from file: 144)
DIALOG(R)File 144:Pascal

14677854 PASCAL No.: 00-0351424
New drugs for hepatitis C virus (HCV)
Hepatitis C
CLARKE B E
FOSTER G R, ed
Virology Research Unit, GlaxoWellcome Medicine Research Centre, Gunnels Wood Road, Stevenage, Hertfordshire, SGI 2NY, United Kingdom
Department of Medicine, QEQM Wing, St Marys Hospital, London, W2 IPG, United Kingdom
Journal: Bailliere's best practice & research. Clinical gastroenterology, 2000, 14 (2) 293-305
Language: English
Lack of efficacy and significant side effects have severely limited the use of interferon-a (IFN-a) as the standard therapy for non-A non-B hepatitis (NANBH) caused by hepatitis C virus (HCV) and alternative, improved therapies are urgently sought. Attempts have been made to improve the potency and tolerability of IFN-a by adjusting dosing regimens, methods of delivery and length of treatment. Furthermore, a number of different agents have been used in combination with IFN-a and, from these studies, therapeutic options have been galvanized by the synergistic effects of IFN-a and *ribavirin* . Nevertheless, the majority of patients with HCV still do not sustain lasting therapeutic benefit from this combination and continuing research is required to identify new therapeutic candidates that will have more potent anti-viral activity and less severe side effects. This review focuses on the progress that has been made in this area and the prospects for new effective therapies in the near future.

6/AB/34 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10525621 20417957
A dose-ranging study of *pegylated* *interferon* *alfa*-2b and *ribavirin* in chronic hepatitis C. The Hepatitis C Intervention Therapy Group.
Glue P; Rouzier-Panis R; Raffanel C; Sabo R; Gupta SK; Salfi M; Jacobs S; Clement RP
Schering-Plough Research Institute, Kenilworth, NJ. paul.glue@spcorp.com
Hepatology (UNITED STATES) Sep 2000, 32 (3) p647-53, ISSN 0270-9139 Journal Code: GBZ
Languages: ENGLISH
Document type: CLINICAL TRIAL; JOURNAL ARTICLE; RANDOMIZED CONTROLLED TRIAL
The objectives of this study were to assess the safety, pharmacokinetics, and efficacy of *pegylated* *interferon* *alfa*-2b (*PEG*-Intron) plus *ribavirin* in patients with chronic hepatitis C. A total of 72 patients (35 men/37 women, age range 20-68 years) with clinically compensated chronic hepatitis C virus (HCV) were enrolled into this open-label, randomized, active controlled study. Patients received either *PEG*-Intron 0.35, 0.7, or 1.4 &mgr;g/kg subcutaneously weekly for 24 weeks alone, or in combination with *ribavirin* 600, 800, or 1,000 to 1,200 mg orally daily. Patients were evaluated during treatment and after a 24-week follow-up period for safety and efficacy. Detailed pharmacokinetic assessments were performed at weeks 1 and 4. *PEG* -Intron alone produced expected dose-related reductions in white cells, neutrophils and platelets. Addition of *ribavirin* reduced hemoglobin levels in a dose-related manner, did not further reduce *PEG*-Intron-induced decreases in neutrophil or white cell count, and increased platelet counts. Neutrophil function tests (C5a and FMLP migration, killing curves) were unaltered. Reported adverse events (flu-like symptoms, asthenia) were qualitatively similar in all dose groups. Anti-HCV activity, as measured by loss of detectable serum HCV RNA (i.e. <100 copies/mL) at the end of treatment (week 24) and after 24 weeks of follow-up (week 48) showed dose-response trends for *PEG*-Intron. At each *PEG* -Intron dose level, anti-HCV activity was higher in patients coadministered *ribavirin* than in patients treated with *PEG*-Intron monotherapy. There was no evidence of pharmacokinetic interactions with either drug. We conclude that the safety and tolerability of combined *PEG* -Intron/*ribavirin* and *PEG*-Intron alone were comparable. Combined *PEG* -Intron/*ribavirin* showed dose-related synergistic anti-HCV effects, which were numerically superior to those obtained with *PEG*-Intron monotherapy.

6/AB/35 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10335100 20184082
Interferon and *ribavirin* combination therapy: indications and schedules.
Weiland O
Division of Infectious Diseases I73, Huddinge Hospital and Karolinska Institute, Huddinge, Sweden.
Forum (ITALY) Jan-Mar 2000, 10 (1) p22-8, ISSN 1121-8142

Journal Code: C0R
Languages: ENGLISH
Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL
Treatment outcome for patients with chronic hepatitis C virus infection has greatly improved during the last years with the development of interferon (IFN) and *ribavirin* combination therapy. The final decision to treat or not, however, is complex and should be based on several factors such as the age of the patient, the general health, the risk of developing cirrhosis and the probability of a cure with treatment. Combination therapy with standard doses (IFN-a 3 x 106 IU three times per week plus *ribavirin* 1000-1200 mg daily in two divided doses) for six (up to 12) months significantly improves the sustained biochemical and virological response rates 2-3 times as compared to IFN alone given during 12 months. Combination therapy has thus become standard therapy for na ve patients and relapse patients after a prior IFN treatment course. For patients with favourable baseline viral characteristics (genotype 2 and 3 irrespective of viral load) six months combination therapy is sufficient whereas patients with unfavourable viral baseline characteristics (genotype 1 with high baseline viral load) will need 48 weeks combination treatment. In addition, for patients with compensated cirrhosis, combination therapy is superior and better tolerated than IFN monotherapy. For the future better optimised treatment schedules and dosing regimens for IFN in combination with *ribavirin* need to be worked out and individualised according to genotype to further improve treatment results. Utilisation of new IFN formulas such as *pegylated* IFN and consensus IFN in combination regimens will probably improve treatment further.

6/AB/36 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10265367 20079345
Therapy of special HIV-associated diseases: HCV-HIV-co-infection and AIDS-related Kaposi's sarcoma - official satellite to the 7th European Conference on Clinical Aspects and Treatment of HIV-infection, October 23, 1999 in Lisbon, Portugal.
Goebel FD; Jablonowski H
Medizinische Poliklinik der Universitat Munchen, Pettenkoferstr. 8a, D-80336 Munchen, Germany. goebel@pk-i.med-uni-muenchen.de
European journal of medical research (GERMANY) Dec 16 1999, 4 (12) p507-13, ISSN 0949-2321 Journal Code: COQ
Languages: ENGLISH
Document type: CLINICAL TRIAL; CLINICAL TRIAL, PHASE III; CONGRESSES; RANDOMIZED CONTROLLED TRIAL
BACKGROUND: In the era of highly active antiretroviral therapy (HAART), certain complications of HIV-disease as e.g. opportunistic infections and Kaposi s sarcoma (KS) have significantly diminished. New insights in pathological pathways revealed the role of co-viruses as HHV-8 and HCV so that in our days AIDS-associated KS and chronical hepatitis C (CHC) in HIV-infected persons can be considered as the result of opportunistic infections with HHV-8 or HCV respectively. - Though the overall incidence of AIDS-KS is declining, it remains as a reason of severe disease complication and fatal outcome. Actual therapeutic strategies have to be evaluated regarding safety and efficacy as a major option, while cost-effectiveness of treatment and quality of life aspects for the patient must also be included to assess a successful disease management within the up to now merely palliative setting. HIV-infection evidently triggers the natural course of CHC in terms of more progressive liver disease. Otherwise there seems to be no clinical benefit of HAART on CHC. Until recently

IFN-alfa treatment was the only therapy available for patients with CHC. As initial therapy with a combination of IFN-alfa and *ribavirin* turned out to be more effective than IFN-monotherapy in HCV-infected persons, it has now to be considered to include anti-HCV-combination treatment into the therapeutic program of HIV-HCV-coinfected patients under HAART. - Within the 7th European Conference on Clinical Aspects and Treatment of HIV-Infection, which took place in Lisbon from October 23 to 27 1999, a satellite symposium was organized to evaluate actual treatment options in the management of special HIV-associated complications focussing on AIDS-KS and HCV-HIV-coinfection. METHODS: To evaluate the safety and efficacy of IFN-alfa-2b and *ribavirin* combination therapy in patients with CHC, a total of 1773 treatment-naive patients was recruited in two phase III clinical trials. They were randomized in 4 treatment schedules to receive IFN-alfa-2b plus *ribavirin* or placebo for 24 weeks or 48 weeks respectively. Cost-effectiveness data compared treatment with liposomal daunorubicin and *pegylated* liposomal doxorubicin in AIDS-KS-patients within two phase III studies. The assumptions were a comparable efficacy, gastrointestinal toxicity, and frequency of opportunistic infections (OI). A quality-of-life-study on KS-treatment with *pegylated* liposomal doxorubicin (PLD, Caelyx(R)) was based on a phase III study with an overall median survival of 160 days for the patients, who completed questionnaires with 30 items specific for HIV-related diseases. The health-related quality-of life (HRQL) assessment and analysis includes 11 domains, in which improvements were calculated within a multiple analysis to be significant if they are higher than 10 (at a 0-100 scale). RESULTS: In 1775 treatment-naive patients with CHC, response rates to a combination therapy of IFN-alfa-2b with *ribavirin* was significantly higher in all patient groups with more than 60% of sustained virological response in patients with genotype 2 and 3, while patients with genotype 1 (poorer prognosis) benefit from extended duration from 24 to 48 weeks (17% versus 29% of sustained virological response). - *Pegylated* liposomal doxorubicin (PLD, Caelyx(R)) in the treatment of AIDS-related KS is more effective and less toxic than BV or ABV. Cost-effectiveness analysis suggests that PLD is preferable over liposomal daunorubicin, BV and ABV. Regarding the HRQL-assessment, PLD came out to be superior in 9 of 11 domains tested, with the greatest improvement in general health and pain relief. CONCLUSIONS: As the combination therapy of IFN-alfa-2b with *ribavirin* is the first treatment in CHC, there is an urgent need to consider the therapeutical strategies in this field in HCH-HIV coinfected patients. (ABSTRACT TRUNCATED)

6/AB/37 (Item 1 from file: 351)
DIALOG(R)File 351:Derwent WPI

013415316
WPI Acc No: 2000-587254/200055
XRAM Acc No: C00-175086
Use of a *pegylated* *interferon*-*alpha* for treating HIV-1 patients, especially those co-infected with hepatitis C
Patent Assignee: SCHERING CORP (SCHE)
Inventor: GLUE P W; LAUGHLIN M A; STALGIS C O
Number of Countries: 089 Number of Patents: 003
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 200051631	A2	20000908	WO 2000US5361	A	20000301	200055	B
EP 1034790	A2	20000913	EP 2000301695	A	20000302	200055	
CA 2299893	A1	20000902	CA 2299893	A	20000301	200059	

Priority Applications (No Type Date): US 99454004 A 19991203; US 99260388 A 19990302; US 99268521 A 19990312; US 99288358 A 19990408
Patent Details:
Patent No Kind Lan Pg Main IPC Filing Notes
WO 200051631 A2 E 45 A61K-038/21
Designated States (National): AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CZ DE DK DM EE ES FI GB GD GE HR HU ID IL IN IS JP KG KR KZ LC LK LR LT LU LV MA MD MG MK MN MX NO NZ PL PT RO RU SE SG SI SK SL TJ TM TR TT TZ UA US UZ VN YU ZA
Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
EP 1034790 A2 E A61K-038/21
Designated States (Regional): AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
CA 2299893 A1 E A61K-038/21

Abstract (Basic): WO 200051631 A2
Abstract (Basic):
NOVELTY - Use of a *pegylated* *interferon*-*alpha* for preparation of a medicament for treating human immuno-virus-1 (HIV-1) infections, is new.
(N.B. ''*Pegylated* *interferon*-*alpha*'' indicates *polyethylene* *glycol* modified conjugates of *interferon*-*alpha*).
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for the use of an anti-HIV-1 drug therapy and *pegylated* *interferon*-*alpha* for the preparation of a medicament for treating HIV-1 infections.
ACTIVITY - Anti-HIV; Virucide; Hepatotropic
Tests are described but no results are given.
USE - The methods are for the treatment of adult and pediatric HIV-1 patients, especially those co-infected with HCV.
ADVANTAGE - The methods aim to lower detectable HIV-1 RNA in patients.
pp; 45 DwgNo 0/0

6/AB/38 (Item 2 from file: 351)
DIALOG(R)File 351:Derwent WPI

013270634
WPI Acc No: 2000-442540/200038
XRAM Acc No: C00-134661
Use of *ribavirin* and *pegylated* *interferon* *alpha* for treatment of chronic hepatitis C comprises administration in two specific time periods
Patent Assignee: SCHERING CORP (SCHE)
Inventor: ALBRECHT J K; GLUE P W
Number of Countries: 087 Number of Patents: 002
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 200037110	A2	20000629	WO 99US27935	A	19991216	200038	B
AU 200021570	A	20000712	AU 200021570	A	19991216	200048	

Priority Applications (No Type Date): US 98215876 A 19981218
Patent Details:
Patent No Kind Lan Pg Main IPC Filing Notes
WO 200037110 A2 E 33 A61K-047/48
Designated States (National): AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CZ DE DK DM EE ES FI GB GD GE HR HU ID IL IN IS JP KG KR KZ LC LK LR LT LU LV MA MD MG MK MN MX NO NZ PL PT RO RU SE SG SI SK SL TJ TM TR TT

TZ UA UZ VN YU ZA
Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
AU 200021570 A A61K-047/48 Based on patent WO 200037110

Abstract (Basic): WO 200037110 A2
Abstract (Basic):
NOVELTY - The use of *ribavirin* (I) and *pegylated* *interferon* *alpha* (II) for the preparation of a composition for treating a patient suffering from chronic hepatitis C infection to eradicate detectable HCV (hepatitis C virus)-RNA, is new and comprises administering (I) and (II) in two treatment time periods.
DETAILED DESCRIPTION - The use of *ribavirin* (I) and *pegylated* *interferon* *alpha* (II) for the preparation of a composition for treating a patient suffering from chronic hepatitis C infection to eradicate detectable HCV (hepatitis C virus)-RNA, is new and comprises administering (I) and (II) in two treatment time periods:
(a) (I) and an induction dosing amount of (II) are administered for a period to substantially lower detectable HCV-RNA serum levels; and
(b) (I) and (II) are administered for a period of 20 - 30 weeks to eradicate detectable HCV-RNA at least 20 - 30 weeks after the end of (a) and to maintain no detectable HCV-RNA for at least 24 weeks after the end of (b).
An INDEPENDENT CLAIM is also included for the use of (I) and (II) for the preparation of a composition for treating a patient suffering from chronic hepatitis C infection to eradicate detectable HCV-RNA, comprising administering (I) and (II) in two treatment time periods:
(a) (I) and an induction dosing amount of (II) are administered for a period to eradicate detectable HCV-RNA; and
(b) (I) and (II) are administered for a period of 20 - 30 weeks to maintain no detectable HCV-RNA at least 20 - 30 weeks after the end of (a) and to maintain no detectable HCV-RNA for at least 24 weeks after the end of (b).
ACTIVITY - Virucide; hepatotropic; antiinflammatory.
MECHANISM OF ACTION - Viral replication inhibitors.
USE - The methods are used to eradicate or substantially lower detectable HCV-RNA levels and therefore are useful for treating patients suffering from chronic hepatitis C infection (claimed).
ADVANTAGE - The methods provide an improved therapy over prior art for treating chronic hepatitis C patients and for producing a sustained virological response 24 weeks after treatment in a greater number of patients.
pp; 33 DwgNo 0/0

6/AB/39 (Item 3 from file: 351)
DIALOG(R)File 351:Derwent WPI

013270626
WPI Acc No: 2000-442532/200038
XRAM Acc No: C00-134653
Use of interleukin-10 for improving liver histology in difficult to treat patient having chronic hepatitis C virus infection
Patent Assignee: SCHERING CORP (SCHE)
Inventor: DAVIS G L; GRINT P C; NELSON D R
Number of Countries: 087 Number of Patents: 002
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 200037096	A2	20000629	WO 99US27952	A	19991220	200038	B

AU 200021580 A 20000712 AU 200021580 A 19991220 200048

Priority Applications (No Type Date): US 99425716 A 19991022; US 98218842 A 19981222; US 99293742 A 19990416
Patent Details:
Patent No Kind Lan Pg Main IPC Filing Notes
WO 200037096 A2 E 21 A61K-038/20
Designated States (National): AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CZ DE DK DM EE ES FI GB GD GE HR HU ID IL IN IS JP KG KR KZ LC LK LR LT LU LV MA MD MG MK MN MX NO NZ PL PT RO RU SE SG SI SK SL TJ TM TR TT TZ UA UZ VN YU ZA
Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
AU 200021580 A A61K-038/20 Based on patent WO 200037096

Abstract (Basic): WO 200037096 A2
Abstract (Basic):
NOVELTY - Use of interleukin-10 is claimed in a composition for improving liver histology and liver function, for treating and/or preventing liver damage and/or hepatic fibrosis and for modulating the inflammatory response and the fibrosis process responsible for destruction of the liver in a difficult-to-treat patient afflicted with a chronic hepatitis C virus infection.
ACTIVITY - Antiviral.
MECHANISM OF ACTION - None given.
USE - Used for treating liver damage in difficult to treat patients with chronic hepatitis C virus infections.
pp; 21 DwgNo 0/0

6/AB/40 (Item 4 from file: 351)
DIALOG(R)File 351:Derwent WPI

013178502
WPI Acc No: 2000-350375/200030
Related WPI Acc No: 2000-339641
XRAM Acc No: C00-106527
New *ribavirin* derivatives, useful optionally in combination with *interferon*-*alpha*, for treating chronic hepatitis C *infection*
Patent Assignee: SCHERING CORP (SCHE)
Inventor: BENNETT F; GANGULY A K; GIRIJAVALLABHAN V M; LOVEY R G; MCCORMICK J; SAKSENA A K
Number of Countries: 088 Number of Patents: 002
Patent Family:
Patent No Kind Date Applicat No Kind Date Week
WO 200023455 A1 20000427 WO 99US21450 A 19991014 200030 B
AU 200011976 A 20000508 AU 200011976 A 19991014 200037

Priority Applications (No Type Date): US 98174059 A 19981016
Patent Details:
Patent No Kind Lan Pg Main IPC Filing Notes
WO 200023455 A1 E 88 C07H-019/056
Designated States (National): AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CZ DE DK DM EE ES FI GB GD GE HR HU ID IL IN IS JP KG KR KZ LC LK LR LT LU LV MA MD MG MK MN MX NO NZ PL PT RO RU SE SG SI SK SL TJ TM TR TT TZ UA US UZ VN YU ZA
Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
AU 200011976 A C07H-019/056 Based on patent WO 200023455

Abstract (Basic): WO 200023455 A1
Abstract (Basic):
NOVELTY - *Ribavirin* derivatives (I) and their salts are new.
DETAILED DESCRIPTION - *Ribavirin* derivatives of formula (I) and their salts are new.
at least one of R2, R3, R5=polyalkylene oxide polymer conjugate and at least one of the remaining R2, R3, R5=H, R6(W)xCO, R6(W)xCS, R6(W)xC=NR18, (HO)2PO, R6(W)xPO(OH) or HOSO2 and at least one of R2, R3, R5 is not H;
R6=H, alkyl alkanoyl, aryl, heterocyclyl, cycloalkyl, NR7aR7b, alkenyl or alkynyl, where alkyl, alkanoyl, alkenyl or alkynyl are optionally substituted by halo, phenyl, cycloalkyl, NR7aR7b, OH or alkoxy; or
R6=aryl substituted by phenyl; halo, CN, NO2, OH, R18, CF3, SH, SR7a, SOR7a, NR7aR7b, COOH, CO2-, OR7a, O-M+ or S-M+;
M+=alkali metal;
W=O, NR18 or S;
R7a=H; alkyl, alkanoyl or aryl optionally substituted by phenyl, halo, CN, NO2, OH, COOH or alkoxy;
R7b=H, alkyl, aryl optionally substituted by phenyl, halo, CN, NO2, OH, COOH or alkoxy; or
R7a and R7b taken together with N and one of CHR7a, NR7a, O, S, SO or SO2 form a 5-7-membered ring;
R17=H, OR7a, NR7aR7b, R6(W)xCO, R6(W)xCS, R6(W)xC=NR18, (HO)2PO, R6(W)xPO(OH) or HOSO2;
R18=H, alkanoyl or alkyl;
x=1.
INDEPENDENT CLAIMS are also included for:
(1) *ribavirin* derivatives of formula (II)-(IV).
at least one of R2', R3', R5'=polyalkylene oxide polymer conjugate and at least one of the remaining R2', R3', R5' is a natural or unnatural alpha-amino acid residue;
at least one of R50, R52, R53=polyalkylene oxide polymer conjugate and the remaining 2 of R50, R52, R53=H or polyalkylene oxide polymer conjugate;
R50'=polyalkylene oxide polymer conjugate;
(2) use of (I)-(IV) optionally in combination with *interferon*-*alpha* for treating patients having chronic hepatitis C infection to eradicate detectable HCV-RNA.
ACTIVITY - Antiviral.
USE - (I)-(IV) are used, optionally in combination with an *interferon*-*alpha*, for treating chronic hepatitis C *infection* to eradicate detectable HCV-RNA. Also for treating patients having a susceptible viral infection (all claimed).
pp; 88 DwgNo 0/0

6/AB/41 (Item 5 from file: 351)
DIALOG(R)File 351:Derwent WPI

013167768
WPI Acc No: 2000-339641/200029
Related WPI Acc No: 2000-350375
XRAM Acc No: C00-103094
Use of new and known *ribavirin* derivatives and *interferon*-*alpha* for treating chronic hepatitis C *infection*
Patent Assignee: SCHERING CORP (SCHE)
Inventor: BENNETT F; GANGULY A K; GIRIJAVALLABHAN V M; LOVEY R G; MCCORMICK

J; SAKSENA A K
Number of Countries: 087 Number of Patents: 002
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
WO 200023454	A1	20000427	WO 99US21448	A	19991014	200029 B
AU 200011975	A	20000508	AU 200011975	A	19991014	200037

Priority Applications (No Type Date): US 99348534 A 19990707; US 98174059 A 19981016
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200023454	A1	E	120	C07H-019/056	

Designated States (National): AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CZ DE DK DM EE ES FI GB GD GE HR HU ID IL IN IS JP KG KR KZ LC LK LR LT LU LV MA MD MG MK MN MX NO NZ PL PT RO RU SE SG SI SK SL TJ TM TR TT TZ UA UZ VN YU ZA
Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW

AU 200011975	A			C07H-019/056	Based on patent WO 200023454

Abstract (Basic): WO 200023454 A1
Abstract (Basic):

NOVELTY - Use of *ribavirin* derivatives (I) and *interferon*-*alpha* is claimed for treating chronic hepatitis C infection so that HCV-RNA is not detectable for at least 24 weeks after administration.

DETAILED DESCRIPTION - Use of *ribavirin* derivatives of formula (I) and *interferon*-*alpha* is claimed for treating chronic hepatitis C infection so that HCV-RNA is not detectable for at least 24 weeks after administration.

At least one of R2, R3 or R5=H, R6-(W)x-CO, R6-(W)x-CS-(HO)2PO, R6-(W)x-PO(OH) or HO-SO2, provided that at least 1 of R2, R3 or R5 is not H;

R6=H or alkyl, alkanoyl, alkenyl or alkynyl (all optionally substituted by halo, phenyl, cycloalkyl, NR7aR7b, OH or alkoxy) aryl (optionally substituted by phenyl), heterocyclyl, cycloalkyl, NR7aR7b, halo, CN, NO2, OH, R18, CF3, SH, SR7a, SOR7a, SO2R7a, NR7aR7bCO2H, CO2-, OR7a, O-M+, S-M+, (CHR7a)e-(CH7a)f-COOR7b, (CHR7a)e-(CH2)f-OR7b or (CHR7a)e-(CH2)f-NR7aR7b;

W=O, NR18 or S;

R7a=H or alkyl, alkanoyl (all optionally substituted by phenyl, halo, CN, NO2, OH, COOH or alkoxy) or

NR7aR7b + CHR7a, NR7a, O, S, SO or SO2=5-7 membered ring;

R17=H, OR7a, NR7aR7b, R6-(W)x-CO, R6-(W)x-CS, (HO)2PO, R6-(W)x-PO(OH) or HO-SO2;

R18=H, alkyl, alkanoyl or aryl;

e=0-6;

f=0-10 and

x=0 or 1.

INDEPENDENT CLAIMS are included for *ribavirin* derivatives of formula (II) and their salts.

X=a group of formula (i)-(iv);

R2', R3', R5'=H, R20-(W)x-CO, R20-(W)x-CS or R20-(W')w-PO(OH) and at least one of them is not H;

R20=H, cycloalkyl, heterocyclyl, aryl (optionally substituted), NR21R22 or alkyl, alkanoyl, alkenyl or alkynyl (all optionally substituted), (CHR21)e-(CH2)f-COOR22, (CHR21)e-(CH2)f-OR22 or (CHR21)e-(CH2)f-NR21R22;

W'=O, NR28 or S;

R21=H, Y or alkyl, alkanoyl or aryl (all optionally substituted);

R22=H or alkyl or aryl (both optionally substituted) or

R21 + R22 + N and CHR21, NR21, O, S or SO2=5-7 membered ring;
R27=H, OR21, NR21R22, R20-(W')x-CO, R20-(W')-CS, (HO)2PO or R20-(W')x-PO(OH) or HO-SO2;
R28=H, alkanoyl, aryl or alkyl;
at least one of R50', R30' and R20'=Q-(CR51R52)k-CO and the others are H or Q-(CR51R52)k-CO;
Q=C(R53)(R54)(NR55R56);
R51, R52=H or alkyl, alkenyl, alkynyl, 3-7C cycloalkyl or arylalkyl (all optionally substituted) or
CR51R52=cyclopropane, cyclobutane, cyclopentane or cyclohexane;
R53, R54=H or alkanoyl, alkyl, aryl, alkenyl, alkynyl or alkanoyl (all optionally substituted), indol-3-ylmethyl, 4-hydroxyphenylmethyl, imidazol-4-ylmethyl or a group of formula (v);
R57=H or alkyl, alkanoyl, alkenoyl, aryl, arylalkyl, alkenyl or alkynyl (all optionally substituted);
R58=H, alkyl, aryl, arylalkyl, alkenyl or alkynyl;
q=0, 1 or 2;
k=1 or 2;
at least one of R50'', R30'' and R20''=T-(CR58R59)d-CO and the others are H or T-(CR58R59)d-CO;
T=e.g: H2NCH2, H2N(CH2)4 or Me(CH)(OH)CH(H2N), etc;
R58, R59=H or alkyl, alkenyl, alkynyl, 3-7C cycloalkyl or arylalkyl (all optionally substituted) or
CR58R59=cyclopropane, cyclobutane, cyclopentane or cyclohexane;
d=0-2;
R20aCO=+H3N-CO and
Y=e.g: H, Me, HOOCCH2, HOCH2 or 4-hydroxyphenylmethyl, etc.
ACTIVITY - Antiviral.
MECHANISM OF ACTION - None given.
USE - Used for treating viral infections including influenza A and B viral infections, parainfluenza viral infections, respiratory syncytial virus infections, measles viral infections, Lassa fever viral infections, Korean hemorrhagic fever infections, hepatitis B viral infections, Crimean Congo hemorrhagic and HCV infections and HIV-1 infections, encephalitis infections and viral infections in immunocomprised patients. (I) and (II) Metabolize into *ribavirin* in vivo.
ADVANTAGE - Side effects are reduced.
pp; 120 DwgNo 0/0

6/AB/42 (Item 6 from file: 351)
DIALOG(R)File 351:Derwent WPI

013157038
WPI Acc No: 2000-328911/200028
XRAM Acc No: C00-099643
New biheterocyclic compounds are serine protease inhibitors used for treating hepatitis C viral infections
Patent Assignee: AXYS PHARM INC (AXYS-N)
Inventor: HATAYE J M; RICE K; SHELTON E J; SPENCER J R; WANG V R
Number of Countries: 087 Number of Patents: 002
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 200020400	A1	20000413	WO 99US22850	A	19991004	200028	B
AU 200010990	A	20000426	AU 200010990	A	19991004	200036	

Priority Applications (No Type Date): US 98103085 A 19981005
Patent Details:

Patent No Kind Lan Pg Main IPC Filing Notes
WO 200020400 A1 E 55 C07D-235/04
Designated States (National): AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW
Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
AU 200010990 A C07D-235/04 Based on patent WO 200020400

Abstract (Basic): WO 200020400 A1
Abstract (Basic):

NOVELTY - Biheterocyclic compounds (I) are new.

DETAILED DESCRIPTION - Biheterocyclic compounds of formula (I) and their N-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers, mixtures of isomers and salts are new.

n1=0-4;

n2=0-3;

A + B and C + B=fused heterobicyclyl containing 8-12 ring atoms in which each ring contains 5-7 ring atoms with each atom optionally comprising a heteroatom;

X1=N, NR5, O or S;

X5=N, NR6, O or S;

R5=H or 1-6C alkyl;

R6=H or 1-8C alkyl optionally substituted by 1-2 halo, tri-(1-6C) alkylammonium, NR7R7, CONR7R7, OR7, COOR7, OCOR7 or SO2OR7;

R7=H or 1-6C alkyl;

X3=O, S, SO, SO2, CO, NR8 or CR8R9;

R8, R9=H, halo or 1-6C alkyl or

R8 + R9=1-6C alkylidene, in which any 1-3C atoms with a free valence are optionally substituted by halo, tri-(1-6C) alkylammonium, NR10R10, CONR10R10, OR10, COOR10, OCOR10;

R10=H or 1-6C alkyl;

R1, R2=1-6C alkyl, 1-6C alkyloxy, 1-6C alkanoyloxy, 1-6C alkylthio, halo, hydroxy or mercapto and is bonded to any ring C atom in ring B (for R1) or ring C (for R2) with a free valence;

R3=CN, R11, CR12R12NR11R13, C(NR13)R11, COR11, C(NR13)NR11R13, CONR11R13, COOR11, SOR11, SO2R11, SO2NR11R13 or SO2OR11 and is bonded to any C atom in ring B with a free valence;

R11=H, 1-6C alkyl, 3-6C cycloalkyl-(0-3C) alkyl, 3-6C heterocycloalkyl-(0-3C) alkyl, 6-10C aryl-(0-3C) alkyl, 5-14C heteroaryl-(0-3C) alkyl, 9-10C polycycloalkyl-(0-3C) alkyl or 8-10C heteropolycyclo-(0-3) alkyl (in which all alkyl are optionally substituted by 1-3 P(O)(OR14)OR14, SO2OR14 or COOR14 and any 1-3 ring C atoms with free valences of any aromatic ring are optionally substituted by halo, NO2, CN, optionally halo-substituted 1-6C alkyl, OR14, COOR14, CONR14R14, X6NR14R14, X6NR14CONR14R14 or X6NR14C(NR14)NR14;

X6=a bond or methylene;

R14=H or 1-6C alkyl;

R12=H or 1-3C alkyl or

CR12R12=cyclopropyl;

R13=H or 1-6C alkyl or

R4=R15, OR15, NR15R16, SR15, SOR15, SO2R15, SO2OR15, SO2NR15R16, N(R16)SO2R15, COR15, COOR15, CONR15R16, N(R16)COR15, OCONR15R16, N(R16)COOR15 or N(R16)CONR15R16 bonded to any ring C atom with a free valence in ring C;

R15=1-6C alkyl substituted by 1-2 P(O)(OR17)OR17 or SO2OR17 and optionally substituted by 1-2 COOR17;

R17=H or 1-6C alkyl and

R16=H or 1-6C alkyl.
N.B: X2 and X4 are not defined.
ACTIVITY - Antiviral.
MECHANISM OF ACTION - Serine protease inhibitor; hepatitis C virus protease NS3 inhibitor.
A mixture of HCV NS3 protease (1-3 nM), NS3 cofactor NS4a (10 micro-M), zinc chloride (5 micro-M), tris-(hydroxymethyl)aminomethane (Tris) (50 micro-M), glycerol (50%), Tween 20 (RTM: polyoxyethylenesorbitan monolaurate, 0.05%) and 2-((2-(5-Carbamoyl-1H-benzoimidazol-2-ylmethyl)-3-methyl-3H-benzoimidazole-5-carbonyl)-amino)-phosphono-propionic acid (Ia) was incubated at room temperature for 15 minutes. The quenched fluorescence substrate acetyl-Asp-Glu-Asp(Edans)-Glu-Glu-Abu-T(COO)-Ala-Ser-Lys(Dabcyl)-NH2 was added to a final concentration of 1.5 micro-M. *Hydrolysis* of the fluorescent substrate was followed spectrophotometrically at 485 nm after excitation at 355 nm. Apparent inhibition constants (Ki) were calculated from progress curves of the velocity of the NS3-catalyzed *hydrolysis*.
(Ia) exhibited a Ki value of 0.062 micro-M.
USE - Used for treating hepatitis C virus infection, to prevent the disease occurring in patients predisposed to the disease, but not yet experiencing or displaying the pathology and/or symptoms, to inhibit the disease by arresting development of its pathology and/or symptoms, and to ameliorate the disease by reversing its pathology and/or symptoms.
ADVANTAGE - (I) Are low molecular weight, non-peptide inhibitors of NS3 serine protease.
pp; 55 DwgNo 0/0

6/AB/43 (Item 7 from file: 351)
DIALOG(R)File 351:Derwent WPI

013145982
WPI Acc No: 2000-317854/200027
XRAM Acc No: C00-096220
Treatment of HIV infection comprises administration of a cytotoxic agent and at least one non-nucleoside reverse transcriptase HIV inhibitor
Patent Assignee: DU PONT PHARM CO (DUPO)
Inventor: KORANT B D
Number of Countries: 046 Number of Patents: 002
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 200021565	A1	20000420	WO 99US23192	A	19991005	200027	B
AU 9965088	A	20000501	AU 9965088	A	19991005	200036	

Priority Applications (No Type Date): US 98103922 A 19981013
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200021565	A1	E	31	A61K-045/06	

Designated States (National): AL AU BR CA CN CZ EE HU IL IN JP KR LT LV MK MX NO NZ PL RO RU SG SI SK TR UA VN ZA
Designated States (Regional): AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

AU 9965088	A		A61K-045/06	Based on patent WO 200021565

Abstract (Basic): WO 200021565 A1
Abstract (Basic):
NOVELTY - Treatment of HIV infection comprises administration of a

cytotoxic agent and at least one non-nucleoside reverse transcriptase HIV inhibitor (NNRTI).

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(a) a kit for the treatment of HIV infection comprising at least one cytotoxic agent, at least one NNRTI and at least one carrier;

(b) a method of eradicating virally infected cells comprising administering a combination of at least one antiviral agent and at least on cytotoxic agent, provided that the antiviral agent is selective for the virus infecting the cells to be eradicated;

(c) a kit for the treatment of chronic viral infection comprising at least one antiviral agent, at least one cytotoxic agent and at least one carrier.

ACTIVITY - Antiviral.

USE - For eradicating virally infected cells, including cells infected with HIV. In (b), the chronic virus infecting the cells is selected from herpesvirus types I and II, cytomegalovirus, hepatitis B virus, hepatitis C virus and varicella-zoster.

ADVANTAGE - The cytotoxic agent and the antiviral or NNRTI agent have a synergistic effect (claimed).

pp; 31 DwgNo 0/0

6/AB/44 (Item 8 from file: 351)
DIALOG(R)File 351:Derwent WPI

012806591
WPI Acc No: 1999-612821/199953
XRAM Acc No: C99-178594
Use of *ribavirin* and/or *interferon*-*alpha* for composition for treating chronic hepatitis C
Patent Assignee: SCHERING CORP (SCHE)
Inventor: ALBRECHT J K
Number of Countries: 084 Number of Patents: 003
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
EP 956861	A1	19991117	EP 99303729	A	19990513	199953	B
WO 9959621	A1	19991125	WO 99US7037	A	19990513	200003	
AU 9938600	A	19991206	AU 9938600	A	19990513	200019	

Priority Applications (No Type Date): US 9879566 A 19980515
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
EP 956861	A1	E	26	A61K-038/21	
	Designated States (Regional): AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI				
WO 9959621	A1	E		A61K-038/21	
	Designated States (National): AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GD GE HR HU ID IL IN IS JP KG KR KZ LC LK LR LT LU LV MD MG MK MN MX NO NZ PL PT RO RU SE SG SI SK SL TJ TM TR TT UA UZ VN YU ZA				
	Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW				
AU 9938600	A			A61K-038/21	Based on patent WO 9959621

Abstract (Basic): EP 956861 A1
Abstract (Basic):

NOVELTY - The use of *ribavirin* and/or *interferon*-*alpha* (IFN-*alpha*) for the manufacture of a pharmaceutical composition, for

treating an antiviral treatment naive patient having chronic hepatitis C infection to eradicate detectable HCV-RNA, is new.

DETAILED DESCRIPTION - The use of *ribavirin* and/or *interferon*-*alpha* (IFN-*alpha*) for the manufacture of a pharmaceutical composition, for treating an antiviral treatment naive patient having chronic hepatitis C infection to eradicate detectable HCV-RNA, is new. The method comprises administering *ribavirin* with IFN-alpha for a period of 20-50 weeks. If the antiviral treatment naive patient has an HCV genotype 1 infection, the patient is administered *ribavirin* in association with IFN-alpha for 40-50 (especially 48) weeks and if the antiviral treatment naive patient has an HCV genotype 2 or 3 infection, the patient is administered *ribavirin* in association with IFN-alpha for 20-30 (especially 24) weeks.

ACTIVITY - Antiviral.

A study was carried out to study the effects of administering IFN-alpha with *ribavirin* and IFN-alpha with a placebo. After 24 weeks of treatment, 81% of the group administered with IFN-alpha with *ribavirin* had no detectable HCV-RNA and in the placebo group 48% of the group had no detectable HCV-RNA after a further 4 weeks.

MECHANISM OF ACTION - The combination of *ribavirin* and/or IFN-alpha eradicates detectable HCV-RNA.

USE - The composition of *ribavirin* and/or IFN-alpha is useful for the preparation of a pharmaceutical composition for treating antiviral treatment naive patient having chronic hepatitis C (claimed).

ADVANTAGE - The composition eradicates HCV-RNA in a long-term and effective manner.

pp; 26 DwgNo 0/0

6/AB/45 (Item 9 from file: 351)
DIALOG(R)File 351:Derwent WPI

012639277
WPI Acc No: 1999-445381/199938
XRAM Acc No: C99-131363
Treatment of hepatitis C virus infection and associated liver cancer with *hydrolytic* enzyme and flavonoid
Patent Assignee: MUCOS PHARMA GMBH & CO (MUCO-N)
Inventor: RANSBERGER K; STAUDER G
Number of Countries: 025 Number of Patents: 002
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
DE 19804742	A1	19990812	DE 1004742	A	19980206	199938	B
EP 943337	A2	19990922	EP 99101335	A	19990125	199943	

Priority Applications (No Type Date): DE 1004742 A 19980206
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
DE 19804742	A1		10	A61K-038/46	
EP 943337	A2	G		A61K-038/48	

Designated States (Regional): AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
Abstract (Basic): DE 19804742 A1
Abstract (Basic):

NOVELTY - The use of at least one *hydrolytic* enzyme (I) and at least one flavonoid (II) to treat diseases caused by the hepatitis C virus is new.

ACTIVITY - Antiviral; anticancer.

MECHANISM OF ACTION - None given.

USE - (I) is used to treat chronic hepatitis C and/or liver cell carcinoma (both claimed). Oral treatment of hepatitis C patients with 90 mg bromelain, 48 mg trypsin and 100 mg rutoside, 3 times per day for 12 weeks markedly reduced activity of liver transaminases (e.g. reduced the liver aspartate aminotransferase activity from circa 123 U/l to circa 68 U/l) and was well tolerated.

ADVANTAGE - The combination of (I) and (II) is more effective than (expensive) previously used drugs (e.g. *alpha*-*interferon* or *ribavirin*) and causes no harmful side effects even on long term use. (I) can be isolated inexpensively from natural materials.

pp; 10 DwgNo 0/7

6/AB/46 (Item 10 from file: 351)
DIALOG(R)File 351:Derwent WPI

012578054
WPI Acc No: 1999-384161/199932
Related WPI Acc No: 1999-384698; 2000-316964
XRAM Acc No: C99-112909
Fast dissolving oral dosage form containing *ribavirin*
Patent Assignee: SCHERING CORP (SCHE)
Inventor: BOWEN F E; CHAUDRY I A; LIEBOWITZ S M; STUPAK E I; VADINO W A; STUPAK E J
Number of Countries: 084 Number of Patents: 009
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
US 5914128	A	19990622	US 97997172	A	19971222	199932	B
WO 9932128	A1	19990701	WO 98US26222	A	19981221	199933	
ZA 9811726	A	19990831	ZA 9811726	A	19981221	199939	
AU 9921991	A	19990712	AU 9921991	A	19981221	199950	
EP 991415	A1	20000412	EP 98965983	A	19981221	200023	
			WO 98US26222	A	19981221		
CA 2300452	A1	19990701	CA 2287056	A	19981221	200036	
			CA 2300452	A	19981221		
CA 2287056	C	20000815	CA 2287056	A	19981221	200050	
			WO 98US26222	A	19981221		
NO 200003234	A	20000821	WO 98US26222	A	19981221	200052	
			NO 20003234	A	20000621		
BR 9814367	A	20001017	BR 9814367	A	19981221	200056	
			WO 98US26222	A	19981221		

Priority Applications (No Type Date): US 97997172 A 19971222; US 97997169 A 19971222
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
US 5914128	A		6	A61K-009/48	
WO 9932128	A1	E		A61K-031/70	

Designated States (National): AL AM AT AU AZ BA BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GD GE HR HU ID IL IN IS JP KG KR KZ LC LK LR LT LU LV MD MG MK MN MX NO NZ PL PT RO RU SE SG SI SK SL TJ TM TR TT UA US UZ VN YU

Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW

ZA 9811726	A		19	A61K-000/00	
AU 9921991	A			A61K-031/70	Based on patent WO 9932128
EP 991415	A1	E		A61K-031/70	Based on patent WO 9932128

Designated States (Regional): AT BE CH DE DK ES FI FR GB GR IE IT LI LT LU LV NL PT RO SE

CA 2300452	A1	E	A61K-031/7056	Div ex application CA 2287056
CA 2287056	C	E	A61K-031/70	Based on patent WO 9932128
NO 200003234	A		A61K-000/00	
BR 9814367	A		A61K-031/70	Based on patent WO 9932128

Abstract (Basic): US 5914128 A

Abstract (Basic):

NOVELTY - Orally administrable solid dosage form contains *ribavirin* (I) and a disintegrant where the composition has a tap density of at least 0.6 g/ml and more than 80 wt.% (I) dissolves in water in 30 minutes.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a rapidly dissolving *ribavirin* composition comprising:

(a) *ribavirin*;

(b) a filler selected from anhydrous lactose, lactose monohydrate, sucrose, mannitol, microcrystalline cellulose, pregelatinized starch, dibasic calcium phosphate dihydrate, calcium sulfate dihydrate and/or calcium sulfate trihydrate;

(c) a disintegrant selected from croscarmellose sodium, sodium starch glycolate, corn starch, pregelatinized starch, sodium carboxymethyl cellulose, potato starch, microcrystalline cellulose, cross linked polyvinyl pyrrolidone, magnesium aluminum silicate, bentonite, alginic acid and alginates; and

(d) a lubricant selected from magnesium stearate, calcium stearate, zinc stearate, talc, propylene glycol, *PEG* 4000, *PEG* 5000, *PEG* 6000 and stearic acid.

The tap density of the compacted composition is at least 0.6 g/ml.

ACTIVITY - Antiviral;

USE - The capsules are used as antiviral agents, particularly in combination with *interferon* *alpha*-2b for treatment of chronic hepatitis C infection.

ADVANTAGE - The composition displays shorter dissolution and disintegration times. The tap density of 0.6 g/ml allows faster filling of capsules in high speed processing plants without the formation of undesirable *ribavirin* polymorphs.

pp; 6 DwgNo 0/0

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